BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 1 1955

STEATORRHOEA*

BY

A. C. FRAZER, M.D., D.Sc., Ph.D., F.R.C.P.

Professor of Pharmacology, University of Birmingham; Consultant Pharmacologist, Birmingham United Hospitals

Steatorrhoea is a descriptive clinical term. It indicates the passage of fluid or semi-fluid, bulky, pale, fatty, and usually offensive stools. It is incorrect to refer to the passage of formed stools as steatorrhoea merely because the stool, on analysis, is found to contain more than the normal amount of fat; indeed, the misuse of this term has led to some confusion. Steatorrhoea is symptomatic of a number of different pathological conditions, and it cannot be regarded as a constant finding in any of them.

Characteristics of the Steatorrhoeic Stool

Volume and Consistency

The normal daily specimen of faeces on our standard diet has a volume of 100–200 ml. In steatorrhoea the volume of the stool may increase to 500–1,000 ml. or more. There is a concomitant increase of dry weight. There are several reasons for this increase in stool volume. In the first place, more fluid may be passed from the ileum, since it is known that water absorption may be delayed or defective in many of these cases; secondly, the time of transit through the colon is often lessened, so that the amount of water absorbed by the large intestine may be reduced. The presence of electrolytes and other absorbable molecules should not interfere seriously with water absorption in the colon, since this organ normally handles such materials. The long-chain fatty acids *per se* do not have any marked effect on the fluid volume of the stool—plenty of fatty acids may be present in formed stools of normal volume. It is possible that some irritant action arises from the presence of excessive amounts of short-chain fatty acids, but no obvious quantitative correlation has been found between these acids in the stools and volume. Tenesmus is not commonly associated with steatorrhoea. It may be tentatively concluded that the increased volume and the fluid consistency of the stools are likely to be due to some increase in the volume of the material passed into the colon from the ileum, coupled with a relatively early emptying of the large bowel. Some slight irritant action may play a part.

Colour of the Stool

The stool is characteristically pale or putty-coloured. Studies of the pigment content indicate that the bile pigment content of the stool may be within normal limits. Strong reduction of bile pigments produces a similar pale putty colour, and the presence of a strong reducing flora due to carbohydrate fermentation is a common feature in steatorrhoea. Administration of antibacterial agents commonly causes darkening of the stools (Anderson *et al.*, 1954). The best explanation at present available, therefore, for the pallor of the steatorrhoeic stool is that it is due to changes in the bile pigments associated with a fermentative intestinal flora.

Types of Fat in the Faeces

The fat in the stools in steatorrhoea may consist of short-chain volatile fatty acids or long-chain fatty acids, soaps, or glycerides, which may be either solid or liquid at room temperature.

Short-chain Fatty Acids.—These are esssentially derived from carbohydrate fermentation. They can be readily removed by steam distillation. They do not contribute to the fatty appearance of the stool, but they may be partly responsible for the offensive odour.

Long-chain Fats.—These are most commonly present as long-chain fatty acids. They may be seen as sheaves of crystals in faecal smears. In certain types of defect and in most severe cases the fat may appear as liquid fat globules, round which clusters of crystals may be collected. In moderately severe cases most of the fatty acids belong to the saturated series, the predominating fatty acids being palmitic and stearic. In more severe cases the quantity of unsaturated fatty acids increases (Weyers and van de Kamer, 1950). Under certain circumstances the fat is present as glycerides instead of fatty acids. This usually indicates faulty pancreatic lipolysis, but extensive hydrolysis of faecal fat may occur in the absence of pancreatic lipase (Cooke *et al.*, 1946).

Quantity of Fat in the Faeces

Short-chain Fatty Acids.—The daily output is normally less than 1 g.; for accurate assessment the stools should be collected into a cold container and refrigerated during storage.

Long-chain Fatty Acids.—These should be assessed on a standard daily dietary fat intake (50–100 g.). We use a method based on that of van de Kamer *et al.* (1949). The total fatty acid is estimated daily and the faecal fat output calculated as a three-day running mean. Normal daily faecal fat output on our standard diet does not exceed 5 g. when averaged over 10 days. The normal level should be estimated for each laboratory for the standard diet used. Typical results under the conditions prevailing in our unit are illustrated in Fig. 1. For comparative purposes it would seem advisable to take some conventional time period for calculation of

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HEPATOGENOUS GROUP

The liver elaborates bile, which plays an important part in the preparative phase of absorption and other aspects of gastro-intestinal function. The full significance of the bile is not yet understood, but bile salts are considered to be the most important constituent from the absorptive point of view. Bile may be excluded from the intestine by obstructive lesions of the biliary tract. Under these circumstances there is considerable interference with absorption. The stools are loaded with fat, but they are usually well formed and may be of a putty-like appearance and consistency. We have recently had the opportunity of studying a child who was diagnosed as suffering from the coeliac syndrome. On further examination it was found that this child had a marked deficiency of bile salts: this defect appeared to have been present from birth (Ross *et al.*, 1955). The hepatogenous group of absorptive defects are only occasionally associated with steatorrhoea.

ENTEROGENOUS GROUP

When the various food materials are prepared for absorption they enter the small-intestinal cells and are passed through into the portal blood or the chyle. A number of factors are concerned in this transport of absorbed food materials through the intestinal wall. If the preparative phase is normal, interference with absorption may be due to a number of causes—access to the intestinal cells may be prevented, some fault may be present in the intestinal cell itself, intestinal motility may be defective, or the pathways leading from the intestine may be blocked. It is not at present possible to distinguish with certainty between these various possibilities, several of which may coexist. We may, however, split the enterogenous group into two parts—according to the association with, or absence of, gross irreversible pathological changes in the intestine.

(A) *Conditions Associated with Gross Irreversible Pathological Changes in the Intestinal Wall.*—In this group we may include regional ileitis, Whipple's syndrome, tuberculous enteritis, scleroderma, and atrophy of the small-intestinal wall in long-standing cases of malnutrition from any cause. Any of these conditions—most of which are rare—may be associated with steatorrhoea.

(B) *Conditions not Associated with Gross Irreversible Pathological Changes in the Intestinal Wall.*—The cases with enterogenous steatorrhoea that fall into this group have certain common features. All these patients exhibit depressed absorptive capacity of the upper small intestine, as shown by delay and depression of the absorption curves for glucose, xylose, fat, and many other substances. Radiographic examination of the upper intestine reveals increased mucus secretion, which causes clumping of a simple barium sulphate suspension; if a non-flocculable opaque medium is used the upper intestine is found to have an abnormal mucosal pattern, and it is often dilated (Frazer, 1952b).

1. *Gluten-induced Enteropathy.*—The coeliac syndrome has been conclusively shown in Holland and England to be due to the presence of wheat gluten in the child's diet (Dicke, 1950; Anderson *et al.*, 1952; Dicke *et al.*, 1953). In a series of 30 children diagnosed clinically as suffering from the coeliac syndrome, all of whom had steatorrhoea, 28 responded to a gluten-free dietary regime. On this treatment these children passed normal stools containing a normal level of fat (Fig. 3); they also showed significant improvement in weight-for-age ratio, in absorptive capacity, and in the radiographic appearance of the small intestine. The reintroduction of gluten into the diet caused deterioration: one of the children tested had been on a wheat-gluten-free diet for four years. Of the two children who did not respond to the gluten-free diet, one was the child with congenital deficiency of bile salts referred to above; the other has not yet been fully characterized (Ross *et al.*, 1955). The precise cause of the response to gluten in coeliac children is still under investigation. Gluten-induced enteropathy is also found in adult patients (Anderson *et al.*, 1954).

2. *Tropical Sprue.*—The gastro-intestinal situation in this condition is similar to that observed in gluten-induced enteropathy. The main differences between the two conditions are that tropical sprue has a peculiar geographical distribution, it occurs in adults rather than children, it is unrelated to dietary gluten, and it is closely associated with folic acid deficiency. The main areas in which sprue is endemic are the Far East, India, and the Caribbean; it is rare in Africa. Even in the endemic areas, however, there are striking local differences: sprue occurs in Hong Kong, but not in Singapore; in Puerto Rico, but not in Jamaica. There is increasing evidence that some dietary factor may be involved and that this may be related to oxidative rancidity of unsaturated fatty acids. This question is being intensively studied by us at the present time. Folic acid deficiency may play an important part in the development of the syndrome: for a number of reasons, however, it seems unlikely that it is a simple dietary deficiency. Some of the patients with tropical sprue of the type we have been studying develop a more chronic form of the syndrome in which folic acid deficiency is no longer a dominant feature. The steatorrhoea in these patients persists even after their removal to a temperate climate. It is possible that some change in the intestinal flora is responsible for the maintenance of the syndrome in these patients. This is supported by the fact that they dramatically recover when treated with antibacterial therapy (Anderson *et al.*, 1954) (see Fig. 4). It is possible that this form of the syndrome provides the link with classical chronic sprue.

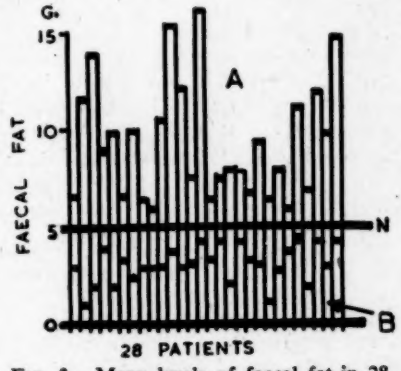

FIG. 3.—Mean levels of faecal fat in 28 consecutive cases of coeliac disease. A=on normal diet. B=on wheat-gluten-free diet. N=normal limit of faecal fat.

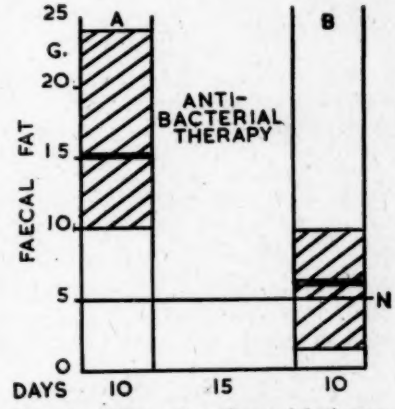

FIG. 4.—Effect of antibacterial therapy on faecal fat level in seven cases of "chronic" tropical sprue (see text). A=before therapy. B=after therapy. The heavy line shows mean value; the shaded area indicates range of values observed.

3. *Non-tropical Sprue.* — Adult patients diagnosed as suffering from non-tropical sprue usually include a significant number of cases of gluten-induced enteropathy. If these are excluded there remains a small group of patients with steatorrhoea, the aetiology of which remains obscure.

4. *Anastomotic Syndrome.* — The possible effect of gastro-enterostomy on the co-ordinated digestion of food in the upper intestinal lumen has already been mentioned. There is, however, another type of surgical case in which steatorrhoea may be the outstanding feature. Gastrocolic or enterocolic fistula and various types of intestinal loop may be associated with steatorrhoea. The precise cause of this is not yet clear, but it is possible that it may be related in some way to the intestinal flora.

Differential Diagnosis

Steatorrhoea may be associated with a number of conditions. Differential diagnosis is important, since different types of treatment are required. The first step is to separate the pancreatogenous, hepatogenous, and enterogenous groups. This is best done by intestinal intubation, as indicated in the Table printed overleaf.

When the pancreatogenous and hepatogenous conditions have been excluded the enterogenous group requires fractionation. Such conditions as Whipple's syndrome, scleroderma, and tuberculous enteritis are rare, and the diagnosis may be reached as a result of associated changes. Regional ileitis can be distinguished from the sprue group by the fact

Investigation of Defects of Intestinal Absorption

Investigation	Expected Results		Enterogenous Group
	Pancreatogenous Group	Hepatogenous Group	
Balance studies:			
Faecal fat	Markedly increased*	Markedly increased*	Increased*
„ nitrogen	Increased	—	May be increased
Short-chain fatty acids	May be increased	—	„ „ „
Intubation studies:			
Pancreatic enzymes	Deficient*	Normal range	Normal range*
Bile salts	Normal range	Deficient*	„ „ „
Absorption curves:			
Glucose	Normal	Normal	Depressed
Chylomicrograph	Flat	Flat	Flattened
Radiography:			
Flocculable media:			
Clumping	Absent	Absent	Present
Mucosal pattern	Feathery	Feathery	Not visible
Non-flocculable media:			
Pattern	„	„	Ladder or coin type
Diameter	Normal	Normal	Dilated

Note.—The results recorded in this Table are the expected findings; some variations will be found, however, in individual patients. The observations marked with an asterisk are the key points in diagnosis.

that the upper intestinal absorptive capacity is usually normal in this condition, and radiographic studies show abnormalities in the lower part of the small intestine. The anastomotic syndromes usually have a surgical history—the fistulous opening may be extremely difficult to demonstrate.

With regard to the three classical varieties of the sprue syndrome, gluten-induced enteropathy is indicated by marked improvement on a gluten-free regime, but it is proved only by demonstrable deterioration when wheat gluten is reintroduced into the diet. In adults it may be necessary to persevere with a gluten-free diet for at least six months before accepting a negative response. It is to be hoped that a quicker method of diagnosis of this condition will be made available soon. The rapid development of the sprue syndrome in a previously healthy adult in an endemic sprue area usually leads to the diagnosis of tropical sprue. Again, a more specific diagnostic test would be advantageous. The haematological changes associated with folic acid deficiency may not appear for some time—indeed, they may not occur at all. Those cases of non-tropical sprue that do not respond to a gluten-free diet must be classified as enterogenous steatorrhoea of unknown aetiology: "non-tropical sprue" would seem to be as good a term as any for this small residual group.

Treatment

There are two main lines of treatment: (1) to cut down intestinal bacterial activity in general and carbohydrate fermentation in particular, and (2) to correct the intestinal absorptive fault, if possible.

General Dietary Regime.—The first of these objectives has formed the basis of treatment for many years. The diet that is usually recommended has a low residue, high protein, and restricted carbohydrate. Some authorities have also advised cutting down fats. There has been fairly general agreement in recent years, however, that a fat intake of 50 g. a day, or even more, is quite well tolerated by most of these patients. The diets recommended by Fairley (1930) for the treatment of tropical sprue form a good basis for the general treatment of the whole group. The proportions of protein/fat/carbohydrate are 1/0.3/1; as improvement occurs, usually after three to four weeks on the high-protein diet, these proportions are stepped up to 1/0.36/2.

Specific Measures

Certain specific measures are effective in steatorrhoea, and they are directed against the main aetiological factors in each case.

Pancreatic Enzyme Deficiency.—In patients with defective pancreatic enzymes some improvement is generally achieved by the administration of pancreatin. The oral administration of pancreatin differs in many respects from the co-ordinated flow of pancreatic juice into the duodenum, so that it is hardly surprising that completely effective replacement is not achieved. One of the best ways of administering pancreatin, especially in children, is to mix the powder in milk, taking care that the milk is not so hot that it damages the enzymes (Ross, 1955). Emulsifying agents may sometimes be helpful in connexion with the absorption of fats and fat-soluble vitamins.

Bile Salt Deficiency.—In the child with deficient bile salts referred to above, the oral administration of bile salts had a dramatic effect on the fat in the stools (Fig. 5). However, on a long-term basis it may be simpler to restrict the fat intake in such cases.

Patients With Gross Pathological Lesions of the Intestine.—Resection of the affected part of the small intestine may be successful in selected cases of regional ileitis. Other cases require general dietary treatment.

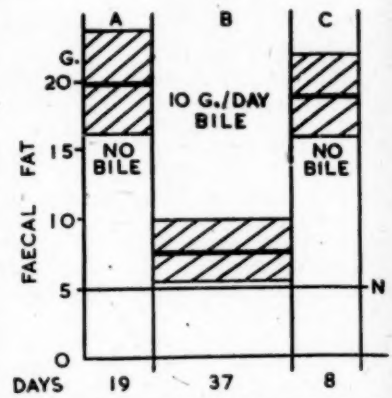

FIG. 5.—Effect of bile on faecal fat level in child with bile salt deficiency. Periods A and C—no bile; period B—oral administration of 10 g. of bile ("desibyl") a day. Heavy line shows mean value for the period; hatched area indicates standard deviation.

Gluten-induced Enteropathy.—These patients must be placed on a wheat-gluten-free diet. This involves the exclusion of a wide range of foods, since wheat flour is widely used in infant foods, pudding mixtures, sauces, soups, confectionery, and custard powders, as well as in bread, cakes, and biscuits. The patient may have any foods that do not contain wheat or rye gluten—including wheat starch. It is important to ensure that the calorie intake is adequate and to keep the protein intake on the high side. In children a response may be expected within six to eight weeks, but in adults the gluten-free diet may have to be continued for six months or more. If vitamin or other deficiencies are present they should be appropriately treated.

Tropical Sprue.—It is probably wise to exclude all fried food from the patient's diet and in severe cases to cut down fat intake. The patient should be treated with folic acid parenterally—5 mg. a day should be adequate. If he does not rapidly respond to treatment he should be removed from the endemic area—preferably to a more temperate climate. Patients that develop the more chronic form which no longer responds to folic acid should be given antibacterial therapy. In the small series here studied various combinations have been used: a five-day course of succinylsulphathiazole 6 g. a day, followed by five days of chloramphenicol, 1.5 g. a day, and then five days of chlortetracycline, 1.5 g. a day, has proved most effective. The final choice of antibacterial agents has not yet been decided; there are a number of objections to the use of chloramphenicol and chlortetracycline. This matter is still under investigation.

Non-tropical Sprue.—Vitamin or other deficiencies should be treated by appropriate replacement therapy. Antibacterial therapy may be dangerous to these patients, especially if the syndrome is one of long standing. It is usually unwise in such cases to attempt to alter the intestinal flora, except by dietary means. Cortisone may be helpful. The beneficial effect is maintained only so long as the therapy is continued.

Anastomotic Syndromes.—These are usually relieved by appropriate surgical treatment. Antibacterial therapy may be useful pre-operatively.

Summary

"Idiopathic steatorrhoea" can now be classified into the pancreatogenous, hepatogenous, and enterogenous groups. The last named can be further differentiated into gluten-induced enteropathy, tropical sprue, or one of the anastomotic syndromes.

Steatorrhoea is taken to mean the passage of loose, bulky, pale, fatty, offensive stools. The steatorrhoeic stool has an increased water content, increased dry weight, normal amount of pigment, which is paler than normal, increased amount of long-chain fatty acids, and increased short-chain volatile fatty acids. The long-chain fatty acids may be of dietary or non-dietary origin, or both. The non-dietary fat may be excreted, or it may be synthesized in the intestine. Increased activity of intestinal organisms may play an important part in the stool changes. Steatorrhoea is, usually, secondary to defective intestinal absorption.

The dietary regime is planned to reduce bacterial activity in the intestine. Specific measures in appropriate cases include replacement of pancreatic enzymes or bile salts, a gluten-free diet, folic acid therapy in early sprue, antibacterial therapy in more chronic cases, and corrective surgery. Cortisone is helpful in some cases of idiopathic steatorrhoea.

References

Anderson, C. M., Frazer, A. C., French, J. M., Gerrard, J. W., Sammons, H. G., and Smellie, J. M. (1952). *Lancet*, **1**, 836.
—— —— —— Hawkins, C. F., Ross, C. A., and Sammons, H. G. (1954). *Gastroenterologia (Basel)*, **81**, 98.
Brain, R. H. F. (1953). *Proc. roy. Soc. Med.*, **46**, 438.
Cooke, W. T., Elkes, J. J., Frazer, A. C., Parkes, J., Peeney, A. L. P., Sammons, H. G., and Thomas, G. (1946). *Quart. J. Med.*, **39**, 141.
Dicke, W. K. (1950). M.D. Thesis, Utrecht.
—— Weijers, H. A., and van de Kamer, J. H. (1953). *Acta paediat. (Uppsala)*, **42**, 223.
Fairley, N. H. (1930). *Trans. roy. Soc. trop. Med. Hyg.*, **24**, 174.
Frazer, A. C. (1952a). *Trans. III Congr. Europ. Soc. Naz. Gastroenterologia*, p. 60.
—— (1952b). *Trans. roy. Soc. trop. Med. Hyg.*, **46**, 576.
Kamer, J. H. van de, Huinink, H. ten B., and Weyers, H. A. (1949). *J. biol. Chem.*, **177**, 347.
Ross, C. A. C. (1955). In press.
—— Frazer, A. C., French, J. M., Gerrard, J. W., Sammons, H. C., and Smellie, J. M. (1955). *Lancet*, **1**, 1087.
Thompson, M. D., and Trowell, H. C. (1952). Ibid., **1**, 1031.
Weyers, H. A., and Kamer, J. H. van de (1950). Centr. Inst. Voedingsonderzoek T.N.O. (Utrecht), Publ. 113.
Weijers, H. A., and Kamer, J. H. van de (1953). *Acta paediat. (Uppsala)*, **42**, 24, 97.
Wollaeger, E. E., Comfort, M. W., and Osterberg, A. E. (1947). *Gastroenterology*, **9**, 272.

A three-and-a-half year study of the physical and mental health of children in Florence is being carried out jointly by Harvard University and the University of Florence. A third interim report was published in November, 1954, at Florence, and describes three projects. The first was to study the influence of a mid-morning half-hour rest, and the second that of a mid-morning snack. Variations of physiological constants were noticed in the course of the morning, but were not affected by a mid-morning rest, while children who had a snack did not have the fall of blood pressure and pulse which appeared in the control children. A decoding test showed that a rest and snack avoided the loss of concentration noticeable at 12.30, when neither was available. The third project was a comparison between classes attending three State elementary schools, one for boys, one co-educational, and one founded by Professor Codignola to provide a less formal education designed to develop initiative. The pupils of the last, though from bad environments and with lower intelligence levels initially, were plainly superior to those of the other two in both intelligence and personality development in the higher classes.

STEATORRHOEA

A REVIEW OF 40 PATIENTS, WITH PARTICULAR REFERENCE TO DIAGNOSIS

BY

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It is generally agreed that the amount of fat in the faeces should not be greater than 10% of the amount of fat ingested each day (Cooke *et al.*, 1946). Steatorrhoea is the term used when this amount is exceeded.

It is convenient to classify steatorrhoea into two main groups: (1) *Primary steatorrhoea*, in which no aetiological factor for the steatorrhoea can be found during life and in which no abnormal underlying disease is found in those cases that come to laparotomy or necropsy. This includes idiopathic steatorrhoea and tropical sprue in adults and coeliac disease in children. Many authors, including Thaysen (1932) and Cooke *et al.* (1953), consider that these three conditions are all manifestations of the same disease process, the aetiology of which is unknown. (2) *Secondary steatorrhoea*, in which a definite lesion that might well cause faulty fat absorption is diagnosed during life, and can always be found at laparotomy or necropsy. This group can be readily subdivided into two: (*a*) cases in which the clinical picture is suggestive of idiopathic steatorrhoea—for example, pancreatitis, post-operative blindloop syndrome; and (*b*) cases with steatorrhoea, but with some other clinically obvious mechanism of disease process—for example, biliary cirrhosis or following pancreatectomy. This subdivision is important, as a differential diagnosis must be made between idiopathic steatorrhoea and cases in group 2*a*.

It was decided to study all the adult cases of steatorrhoea admitted to the Central Middlesex Hospital during the years 1949–54 inclusive, in order to find out the relative frequency of primary and secondary steatorrhoea and to review the diagnostic features. Previously most authors have tended to consider one particular group of steatorrhoea rather than all cases (Thaysen, 1932; Stefanini, 1948; di Sant'Agnese, 1953; Cooke *et al.*, 1953).

We have reviewed the notes of 40 patients admitted during the past six years: the majority of them have been seen personally at some time by one or other of us (Table I). It will be seen that 12 cases have been classified with reasonable certainty as idiopathic steatorrhoea, one case as tropical sprue, and 23 as secondary steatorrhoea; in 4 patients there was insufficient evidence to allow a definite classification into one or the other type.

Idiopathic Steatorrhoea

In establishing that a case of steatorrhoea is in fact idiopathic there are certain characteristic symptoms, signs, and *x*-ray and laboratory findings the assessment of which is necessary before making a final diagnosis.

Weight loss, lassitude, and abdominal discomfort or even pain are frequent symptoms. In contrast to this the weight

Table I.—*Details of 40 Cases of Steatorrhoea*

	No. of Cases
Primary Steatorrhoea	
Idiopathic steatorrhoea	12
Tropical sprue	1
Secondary Steatorrhoea	
(*a*) Clinical picture suggestive of idiopathic steatorrhoea:	
Pancreatic disease:	
Chronic pancreatitis	4
Carcinoma of pancreas	1
Abdominal reticulosarcoma	1
Diverticula of small intestine	1
Intestinal cul-de-sac syndrome	1
Whipple's disease*	1
(*b*) Primary disease clinically obvious:	
Post-gastrectomy:	
Unassociated with gastrocolic fistula	7
Associated " " "	2
Chronic obstructive jaundice:	
Primary biliary cirrhosis	1
Crohn's disease	1
Following jejunostomy	1
Following partial pancreatectomy	1
Thyrotoxicosis	1
Type of steatorrhoea not known	4
Total cases of steatorrhoea	40

* For full description see Avery Jones and Paulley (1949).

is often steady in steatorrhoea due to chronic pancreatitis, in the absence of overt diabetes mellitus (see Case 15). Diarrhoea, although common, is not invariably present, and is often intermittent: Cases 11 and 12, described below, illustrate this. The symptoms of anaemia may be prominent, as may soreness of the tongue if glossitis is present.

A history of childhood diarrhoea may also be of help in confirming the diagnosis. It is important to ask about previous operations in order to differentiate steatorrhoea due to a blind loop of intestine or following a partial gastrectomy.

On clinical examination the patient with idiopathic steatorrhoea is frequently wasted and malnourished, with pigmentation of the skin and glossitis. Hypotension is a common finding, as is abdominal distension. Oedema of the ankles and ascites may occur if the anaemia and malnutrition are severe. In some cases the finger-nails may show koilonychia or clubbing. Examination of the temperature chart will often show a low-grade intermittent pyrexia.

Anaemia is almost invariably found at some stage of the disease, and is often severe. In 10 of our 12 cases the haemoglobin was less than 10 g. per 100 ml., and in three cases less than 5 g. per 100 ml. It is often macrocytic, and so the bone marrow is frequently megaloblastic, and may be indistinguishable from that of pernicious anaemia.

The oral glucose-tolerance curve after the ingestion of 50 g. of glucose is characteristically flatter than normal, and a maximal rise of less than 40 mg. per 100 ml. above the fasting level is often, though not invariably, found. The fractional test meal is of little help in the diagnosis, as any type of curve may be present, although the occurrence of free acid may be helpful in excluding pernicious anaemia in certain cases. The serum calcium level tends to be lowered, and in cases with severe diarrhoea, especially if there is a large volume of fluid stools, the serum potassium may also be low, though this did not occur in any of our cases.

Pancreatic steatorrhoea can best be excluded by the finding of trypsin in the duodenal contents obtained by intubation. This was done in only one of our cases. However, Cooke *et al.* (1953) point out that there are clinical similarities between those cases of idiopathic steatorrhoea that have the presence of pancreatic enzymes proved by duodenal intubation and those in whom this test is not performed. Moreover, in our three fatal cases, which had been diagnosed clinically as idiopathic without pancreatic enzyme studies, no pancreatic or other aetiological factor was present. The nitrogen balance is not a reliable means of distinguishing between these two types of steatorrhoea, as Comfort *et al.* (1953) have shown that nitrogen absorption may be as deficient in idiopathic steatorrhoea as it is in pancreatic steatorrhoea.

It has been pointed out by Wollaeger and Scribner (1951) and by Taylor (1954) that there is a delayed water diuresis in idiopathic steatorrhoea. It is also found in other types of steatorrhoea, but apparently not so constantly, and in other conditions such as renal disease and pernicious anaemia. It shows itself as a nocturnal diuresis, the volume of urine being greater by night than by day. It is suggested that this abnormality is due to delayed absorption of water in the presence of food in the small intestine. While not a diagnostic test, if it is absent it may well be useful in excluding idiopathic steatorrhoea.

Finally, a barium-meal examination of the small bowel may show certain abnormalities in cases of steatorrhoea, including dilatation of the small bowel, thickening of the mucosal folds, and segmentation of the barium. French (1952) suggests that the cause of these abnormalities in idiopathic steatorrhoea is hypersecretion of mucus due to excess of fatty acids in the small bowel. While in itself not a diagnostic feature of idiopathic steatorrhoea, since this "deficiency pattern" may be found in secondary steatorrhoea as well as in other diseases, it often provides useful confirmation. Moreover, it may help to exclude steatorrhoea secondary to a small-bowel lesion.

Tables II and III show the main characteristics of the present series of idiopathic cases. Clearly not all the typical features are found in any one patient, and a diagnosis has to be made by weighing up carefully all the available evidence.

Table II.—*Idiopathic Steatorrhoea*

	No. of Cases
Mode of presentation:	
Diarrhoea	10
Macrocytic anaemia	1
Nocturnal incontinence	1
Other symptoms:	
Appetite—poor	7
" good	3
" not known	2
Lassitude and weakness	6
Weight loss	10
Abdominal pain or discomfort	6
Symptoms of anaemia	6
Childhood diarrhoea	2
Physical signs:	
Abdominal distension	7
Pyrexia (often intermittent)	7
Malnourishment	5
Glossitis	5
Blood pressure less than 110 systolic	5
Skin pigmentation	4
Oedema or ascites	4
Clubbing or koilonychia	3
Total cases	12

Table III.—*Laboratory and X-ray Findings in Idiopathic Steatorrhoea*

	No. of Cases
Anaemia:	
Macrocytic	6
Hypochromic	3
None	1
Type not known	2
Bone marrow:	
Megaloblastic	7
Not known	5
Fat absorption less than 90%	12
Undigested meat fibres in faeces	0
" " " " " not known	6
Serum calcium:	
Less than 4 mEq/litre	4
More " 4 "	6
Not known	2
Oral glucose-tolerance test:	
Less than 40 mg. rise from fasting level	8
More " 40 " " " " "	3
Not known	1
Fractional test meal:	
Histamine-fast achlorhydria	2
Hypochlorhydria	4
Normal	3
Hyperchlorhydria	1
Not known	2
Abnormal excretion of water	2
Not known	10
Barium-meal examination of small bowel:	
Abnormal	7
Normal	1
Not known	4
"Osteoporosis"	5
" not known	7
Total cases	12

Malabsorption of fat is the one constant feature, and the only reliable way of determining this is by means of the three- or four-day fat balance.

It is important to note that diarrhoea is not always a presenting symptom, as is shown in the following two case histories. It may be absent, or have been present intermittently for years and so be regarded by the patient as a "normal" bowel habit. Cooke *et al.* (1953) found that diarrhoea was absent in 20% of their cases.

Case 11

A man aged 36 first attended hospital complaining of nocturnal incontinence of urine: no cause was found. He was next seen two years later complaining of breathlessness, palpitations, and swelling of his ankles. He then admitted that he had had intermittent diarrhoea since childhood. He had been in hospital at the age of 5 for three years with "tuberculous peritonitis," and had also had rickets as a child: in 1939 femoral osteotomy was performed for knock-knee.

On examination he was pale, the fingers were clubbed, and the skin flexures were pigmented; the tongue was smooth, the abdomen was distended, and the ankles were oedematous. Retinal haemorrhages were present; the blood pressure was 120/70. A four-day fat balance showed only 69% absorption. The haemoglobin was 3.7 g. per 100 ml.; M.C.V., 100 cubic microns; M.C.H.C., 31%. The bone marrow was megaloblastic. *X*-ray examination of his knees and wrists showed evidence of old rickets: a plain *x*-ray picture of his abdomen did not reveal any calcified glands. Water-excretion studies showed that he had a nocturnal diuresis, the volume of his night urine being greater than that of his day urine, probably accounting for his nocturnal incontinence. He was treated with folic acid and a high-protein, low-fat diet, and when seen a year later was very well and had no further nycturia or incontinence.

Comment.—This patient illustrates well the abnormal water excretion that occurs in idiopathic steatorrhoea. It is unusual for it to play so prominent a part in the symptomatology that the patient's main complaint is of nocturnal incontinence.

Case 12

A woman aged 65 noticed increasing breathlessness on exertion, with substernal pain; for three weeks she had had swelling of her ankles. Her bowels were open regularly only if she took aperients, though these sometimes caused diarrhoea. Her appetite was poor, but her weight was steady.

Examination revealed that she was very anaemic, with skin pigmentation, a palpable spleen, and oedema of her ankles. Her blood pressure was 125/60 and she ran a low-grade pyrexia. Her haemoglobin was only 3.1 g. per 100 ml.; M.C.V., 109 cubic microns; M.C.H.C., 26%. The bone marrow was megaloblastic and a fractional test meal showed a histamine-fast achlorhydria. A diagnosis of pernicious anaemia was made, and she was treated with injections of vitamin B_{12} and intravenous iron, with a good reticulocyte response. One week after her discharge she developed diarrhoea, with loose watery motions that were difficult to flush away. She was readmitted to hospital, where a four-day fat balance showed only 83% absorption: barium-meal examination of the small bowel showed some clumping of barium, while an oral glucose-tolerance test revealed a maximal rise of only 34 mg. above the fasting level of the blood sugar.

Comment.—It is doubtful whether the correct diagnosis would have been made if the patient had not conveniently developed diarrhoea soon after her discharge from hospital. The anaemia, bone-marrow findings, histamine-fast achlorhydria, and response to treatment were in every respect compatible with a diagnosis of pernicious anaemia.

Secondary Steatorrhoea

It will be seen from Table I that the cases of secondary steatorrhoea outnumber those of the idiopathic type by almost two to one. In fact, there are probably more cases of secondary steatorrhoea admitted to hospital than are diagnosed as such. For instance, most cases of carcinoma of the pancreas come to laparotomy without a preliminary fat balance, and this probably applies to other cases of secondary steatorrhoea, such as regional ileitis. The following cases of secondary steatorrhoea illustrate some of the features important in the differential diagnosis from idiopathic steatorrhoea:

Steatorrhoea Secondary to Chronic Pancreatitis

Case 15.—A man aged 34 had suffered from intermittent attacks of fatty diarrhoea for eight years; his weight was steady and his general health excellent. A four-day fat balance showed only 68% absorption and a nitrogen balance only 71% absorption. His stools contained undigested meat fibres, and trypsin was absent from a sample of duodenal juice. An oral glucose-tolerance test was normal, a plain *x*-ray picture of his abdomen showed widespread pancreatic calcification, and there was segmentation with loss of mucosal pattern on barium-meal examination of the small bowel. Unlike most cases of idiopathic steatorrhoea, there was no anaemia and his nutrition was good. The patient's sister, aged 30, gave a history of "mucous colitis" in the past, although for the last five years she had been perfectly well, with no diarrhoea. She was investigated and also found to have widespread pancreatic calcification, steatorrhoea, absent trypsin in the duodenal juice, and, unlike her brother, impaired carbohydrate tolerance. These two cases clearly show that steatorrhoea *per se* is not necessarily a harmful condition.

Steatorrhoea Secondary to Abdominal Reticulosarcoma

Case 29.—A man aged 60 had a three-months history of a dry skin and a two-months history of diarrhoea and weight loss; his appetite was good but his energy was poor.

On examination he was wasted, with a dry scaly skin, an atrophic red tongue, and angular stomatitis; the abdomen was distended and his blood pressure was 125/70. *X*-ray examination of the chest showed bilateral pulmonary tuberculosis and the sputum was positive for tubercle bacilli. A four-day fat balance showed 55% absorption; the oral glucose-tolerance test was normal; the haemoglobin was 9.9 g. per 100 ml.; M.C.V., 112 cubic microns; M.C.H.C., 35%. Marrow puncture was unsuccessful and the barium-meal examination of the small bowel was normal. He became confused and delirious soon after admission but responded to intensive vitamin therapy. Some weeks later he relapsed and died after appearing to develop signs of Wernicke's encephalopathy. Post-mortem examination confirmed that he had bilateral apical pulmonary tuberculosis; the brain was normal. The mesenteric, retroperitoneal, and parapancreatic lymph nodes were infiltrated with reticulosarcoma and there was one small tumour in the ileum, the remainder of the small intestine being normal.

Comment.—It seems likely that the reticulosarcoma was the primary cause of the steatorrhoea. However, a diagnosis of idiopathic steatorrhoea seemed reasonable at the time considering the general picture, the multiple vitamin deficiencies, and the macrocytic anaemia, together with the absence of any symptoms or signs indicating a primary aetiological cause for the steatorrhoea.

Steatorrhoea Secondary to a Large Intestinal Cul-de-sac

Case 36.—In 1920 a woman, now aged 61, underwent an operation for the removal of Fallopian tubes with abscess formation. In 1946 she had a laparotomy for intestinal obstruction, due to adhesions. These were divided and a side-to-side anastomosis was done in the portion of bowel above and below the obstruction. She remained well until 1952, when she started to lose weight and feel weak. Later she developed numbness and tingling of the hands and feet, a sore ulcerated tongue, and, three months before her admission in 1954, diarrhoea with pale bulky stools, swelling of the legs, and abdominal distension. She also noticed some

unsteadiness when she walked. On examination she was pale but fairly well nourished; her tongue was smooth, the lower abdomen was distended, and there was oedema of the ankles. The blood pressure was 100/60 and there were signs of a sensory peripheral neuritis.

A four-day fat balance showed 78% absorption; the haemoglobin was 8.2 g. per 100 ml.; M.C.V., 133 cubic microns; M.C.H.C., 33%. The bone marrow was partly normoblastic and partly megaloblastic. A fractional test meal showed a histamine-fast achlorhydria, and a glucose-tolerance test was normal. A barium-meal examination showed distension of the small bowel with delay in transit. An injection of 1,000 μg. of vitamin B_{12} raised the haemoglobin to 10.9 g. per 100 ml. She was then given chlortetracycline, 250 mg. four-hourly for ten days; the diarrhoea diminished, and the reticulocyte count rose from 1% to 12% by the eighth day of treatment. She resembled the cases described by Naish and Capper (1953) in whom the anaemia and steatorrhoea were secondary to a stagnant loop of small intestine. At laparotomy there was a greatly dilated blind loop of gut 3 ft. (90 cm.) from the ileocaecal valve, and a resection was done. She made a complete symptomatic and haematological recovery.

Steatorrhoea Secondary to Multiple Jejunal Diverticula

Case 37.—A woman aged 79 presented with weight loss, anorexia, and a history of intermittent attacks of diarrhoea for several years. The stools were formed, pale, and bulky. Ten years previously a macrocytic anaemia had been diagnosed at another hospital and she had had regular injections of liver ever since.

On examination her general condition was good and her blood pressure was 170/95. A barium-meal examination showed multiple large jejunal diverticula. A single 24-hour stool contained 20.7 g. of fat; the haemoglobin was 14 g. per 100 ml.; M.C.V., 112 cubic microns; M.C.H.C., 31%. It seems likely that the steatorrhoea, macrocytic anaemia, and jejunal diverticula are associated. A similar case has recently been reported by Dick (1955). He suggests that stagnation and infection of the diverticula may play some part in the causation of the steatorrhoea and anaemia.

Discussion

The differential diagnosis of the cause of steatorrhoea is of primary importance so far as the treatment of the condition is concerned, for in certain cases of secondary steatorrhoea surgical treatment may be curative. In cases of secondary steatorrhoea with some clinically obvious mechanism of disease process, as in chronic obstructive jaundice, the treatment is that of the primary disease and not of the steatorrhoea, which is merely a symptom; moreover, the differential diagnosis of such conditions from idiopathic steatorrhoea is not difficult.

However, those cases of secondary steatorrhoea with a clinical picture similar to that of idiopathic steatorrhoea, such as the post-operative blind-loop syndrome or pancreatitis, must clearly be differentiated from this condition. The main points of differential diagnosis have already been considered, but certain diagnostically helpful points will be mentioned briefly again. Idiopathic steatorrhoea often presents a definite clinical picture, the correct diagnosis being suggested on these grounds alone. Thus steatorrhoea in a patient who is otherwise fit and well nourished is more suggestive of chronic pancreatitis than of idiopathic steatorrhoea, as in Case 15. Previous history of abdominal operations (Case 36), a history of childhood diarrhoea (Case 11), the presence of a small-bowel lesion on barium-meal examination (Case 37), and tests of pancreatic function (Case 15) may also be useful.

Finally, if there is still some doubt about the aetiology, together with a reasonable chance of a correct diagnosis leading to successful treatment, a laparotomy should be considered: Case 29 partially fits into this category, but a correct diagnosis would only have enabled palliative therapy to be carried out.

Summary

Forty cases of steatorrhoea are reviewed. Of these, 13 were primary steatorrhoea, 23 secondary, and in 4 cases it was not possible to be certain of the type.

The diagnosis of steatorrhoea is discussed, and the importance of excluding an underlying aetiological lesion is emphasized.

Our thanks are due to Dr. F. Avery Jones, under whose care most of the patients were, for his encouragement and advice. Permission to publish cases under their care was kindly given by Drs. R. A. J. Asher, K. P. Ball, and T. D. Kellock.

References

Comfort, M. W., Wollaeger, E. E., Taylor, A. B., and Power, M. H. (1953). *Gastroenterology*, **23**, 155.
Cooke, W. T., Elkes, J. J., Frazer, A. C., Parkes, J., Peeney, A. L. P., Sammons, H. G., and Thomas, G. (1946). *Quart. J. Med.*, **15**, 141.
—— Peeney, A. L. P., and Hawkins, C. F. (1953). Ibid., **22**, 59.
di Sant'Agnese, P. A. (1953). *Pediatrics*, **11**, 224.
Dick, A. P. (1955). *British Medical Journal*, **1**, 145.
French, J. M. (1952). In *Modern Trends in Gastroenterology*, edited by F. Avery Jones, p. 526. Butterworths, London.
Jones, F. Avery, and Paulley, J. W. (1949). *Lancet*, **1**, 214.
Naish, J., and Capper, W. M. (1953). Ibid., **2**, 597.
Stefanini, M. (1948). *Medicine (Baltimore)*, **27**, 379.
Taylor, W. H. (1954). *Clin. Sci.*, **13**, 239.
Thaysen, T. E. H. (1932). *Non-Tropical Sprue*. Copenhagen and London.
Wollaeger, E. E., and Scribner, B. H. (1951). *Gastroenterology*, **19**, 224.

FUNCTIONAL UTERINE BLEEDING*

BY

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Three years ago I was lucky enough to be enabled to visit Canada and the U.S.A. through a grant from my hospital, and it was whilst working in the Royal Victoria Hospital, Montreal, under the ægis of Dr. Newel Philpot that I began to appreciate the importance of the Papanicolaou smear in the routine examination of patients attending the out-patients department and the well women's clinic.

I decided to try, by the use of this technique in my own clinics, to get some rational basis for treatment in cases of uterine bleeding which could not be explained on routine clinical findings, and, further, to check the results of therapy by a series of such smears. I believe I am right in saying that, at the outset, vaginal smears were used to gain some information about ovarian function from the assessment of the cornification, etc., and that cancer detection was a later development.

Through a research fellowship established shortly after my return home, and through the work of my colleague Dr. Mary Egerton, the holder of this fellowship, it has been possible to examine and follow-up a number of patients during the past two and a half years, and it is largely because of this work that I would discuss some aspects of the problem.

Definition

By functional uterine haemorrhage I understand bleeding from the uterus for which no cause can be found in the general condition of the patient, on clinical examination of the pelvic organs, or on curettage of the cavity. This last proviso requires some amplification. I am confident that, in general, a diagnosis of functional bleeding should not be

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accepted without curettage to exclude such conditions as retained products of conception, placental polypi, and, of of course, neoplasms—a small subendometrial fibroid or a carcinoma of the body of the uterus or endocervix. An exception to this proviso might be entertained in the case of an adolescent, provided always that response to treatment was speedy and satisfactory. Otherwise, these patients, too, should be examined under anaesthesia and curetted to confirm the diagnosis fully.

Forms Which Functional Uterine Bleeding May Take

The term "functional uterine bleeding" implies, to my mind, an alteration in the usual cycle of any given patient. Cases where the interval is twenty-one days, cases where the interval is five or six weeks, are known to us all and appear to be normal in the individual; the duration of the flow also varies with the individual, and menstrual periods of two days or seven days would be normal in certain women.

It is with the patients who have a deviation from their own accepted normal that we are here concerned. It is recognized that some girls at puberty do not settle down for a few months to a rhythm which could fall within average limits, but if they do not so settle, or if the flow is so profuse or prolonged as to affect their general condition, then these patients too would fall into the big group under consideration. When these points have been considered and allowed for, functional bleeding may present as: (*a*) menorrhagia—prolonged and/or profuse menstrual periods; (*b*) frequent periods—that is, a definite reduction in the length of the cycle; or (*c*) irregular cycles—sometimes long, sometimes short.

Irregular intermenstrual bleeding is not included, as, with the exception of ovulation bleeding, this symptom usually indicates an abnormality of the pregnant state, or a new growth of the reproductive tract. Also, in my view, postmenopausal bleeding should never be included, though the production of vaginal bleeding in post-menopausal women as a result of the administration of oestrogens, for varied and at times invalid reasons, confuses the issue to a considerable extent and must have led to the performance of a large number of operations for curettage otherwise uncalled for.

The great majority of patients under review sought advice for prolonged and/or profuse menstrual periods, but, in some, irregular periods and shortened cycles were the prominent symptoms.

Procedure

When a patient seeks advice for some symptom falling within the group under consideration, her age and marital status are noted and a careful history is taken with regard to the present symptom or illness; her previous health; her obstetric experience, including pregnancies which have been interrupted by miscarriage, ectopic implantation, or mole formation; the family history; and menstruation.

The blood pressure is recorded, the urine examined, and the haemoglobin estimated. The patient then has a general physical examination, with due regard to the particular importance of diseases associated with hypertension, diseases of the blood, anaemias, and diseases of the endocrine glands—for example, the thyroid. I think, too, that an attempt should be made to assess her nutritional state and her psychological condition. In my experience, menorrhagia is often allied to unsatisfactory contraceptive methods (coitus interruptus) or to disturbed sexual or marital relationships.

Moving now to the more strictly gynaecological field, the abdomen is investigated, the Papanicolaou smear is taken, and the pelvic organs are examined digitally and by speculum. In the present series the Papanicolaou smears have all been taken by a gynaecologist, under direct vision from the posterior fornix and cervix in married and parous women, and by aspiration from the posterior fornix in virgins and children. The smear from the cervix is used for cancer screening and that from the posterior fornix for endocrine estimation. It has not always been possible to take the smear at the most appropriate or advantageous point of the cycle, since the procedure is a routine one in my clinic at the first visit; but, where necessary, the patient has been given an appointment at the correct date and the smears have been repeated. It has occasionally been found necessary to repeat the smear when an overlying discharge due to vaginitis, possibly from a trichomonal infection, or a cervicitis, has obscured the picture.

If on clinical examination no general or local cause has been found to account for the presenting symptom of uterine bleeding, the patient is curetted, the operation being performed in the second half of the cycle. Owing to the severe pressure on hospital accommodation, this procedure has been omitted in a few cases of adolescents and a few adults whose main complaint is an irregular cycle, but curettage and histological examination of the endometrium should be regarded as an integral part of the diagnosis.

By the study of the Papanicolaou smears Dr. Egerton and I have divided our cases of functional bleeding into four groups:

1. *Menorrhagias of Puberty.*—Here the smear shows low hormonal levels but an oestrogen preponderance at low level. There is evidence that the cycle is anovulatory and the endometrium has undergone no distinct pathological changes.

2. *Menorrhagias of Early Reproductive Life.*—These patients are usually between the ages of 20 and 30 years. The hormonal levels are low generally, with no undue preponderance of either hormone. The cycle is ovulatory and the endometrium within normal limits.

3. *Late Reproductive Life (Ages 35–45 Years).*—Here the endometrium deviates from the normal. It may show an exaggerated proliferative phase, or there may be a hyperplastic polypoidal endometrium characterized by distension of the tubular serous-secreting glands and often by small areas of superficial necrosis. But the histological findings on curettage do not give a complete picture, and the smear shows that these cases should be subdivided into (*a*) those with an oestrogen preponderance but evidence of some progesterone effect, with the total hormones at a reduced level; and (*b*) those with a high and persistent oestrogen level. In the first subgroup the patients have an exaggerated proliferative phase in the endometrium, with some secretory effect towards the end of the cycle. In the second subgroup are those cases with a polypoidal endometrium, and in these patients it may be possible to detect follicular retention cysts of the ovary on clinical examination.

4. *Menorrhagias of the Menopause.*—The curettage is typically scanty to the naked eye, but histologically within normal limits. The cycles are anovulatory, and the smear indicates a reduction in hormonal levels but with oestrogen preponderance.

It is of some importance to emphasize that these groups are not necessarily as clear-cut as this arrangement might suggest: there is inevitably some overlapping, but the classification has proved useful in determining treatment, particularly where radical measures are contraindicated.

Treatment

There are, I think, four possible lines of treatment that should be reviewed.

Firstly, simple symptomatic treatment may be considered, and probably will be tried at the onset before a full diagnosis has been made. This treatment would consist of correction of any secondary anaemia and administration of drugs to control the actual flow by acting on the uterine muscle. I am convinced of the importance of dealing with the anaemia, and for this purpose use iron and some form of proteolysed liver together with vitamin B. If, as I believe, the bleeding is due to endocrine disorder, the oxytocic drugs are unlikely to be effectual, and this indeed in practice proves to be the case.

Secondly, there are operative measures. Curettage, apart from its diagnostic importance, is valueless in the first, second, and fourth groups, where the endometrium does not show definite hypertrophic changes. It is, however, of some value in the metropathia group, though usually the improvement is transitory. It is a little difficult to see why

this should be so; but tentatively I suggest that after a thorough curettage the endometrium may not build up to the fully developed polypoidal or hyperplastic state characteristic of this group for several cycles. Even more tentatively I put forward the idea that curettage may stimulate normal ovarian function temporarily and so produce, at least in the younger patients, some progesterone effect in subsequent cycles. Curettage therefore has a place in the management of metropathia in the woman nearly approaching the menopause, when the transitory improvement may tide her over the intervening interval before cessation of the periods. The operation of castration by removal of the ovaries I do not consider. It is obviously contraindicated in adolescents and women under 40, and in the woman over 40 removal of the ovaries and retention of a pathological uterus does not make sense. Personally, I would not accept removal of one out of two comparable ovaries: I can see no logic in this, since experience shows that a patient with one ovary is indistinguishable from a patient with two in respect of her ovarian hormone production. There remains hysterectomy. This should be very seriously considered in women over 45, or even over 40. A dysfunctioning and potentially dangerous organ is removed and the condition is cured. The strongest argument against such treatment is that based on psychological grounds. I submit that such grounds will, in some patients, provide a weighty and valid contraindication to hysterectomy. In my view, when hysterectomy is being carried out for this condition in a woman over 45 the ovaries should be removed. I have not observed more severe menopausal symptoms after this procedure at this age than when the ovaries are left. In women under 45, and provided the ovaries are normal to direct clinical inspection and examination, each case should be dealt with on its merits, but I favour leaving the ovaries as a general rule. In younger patients hysterectomy may be the only means of relieving them of their symptoms and ill-health, but must be regarded as an expression of failure in both diagnosis and treatment.

Thirdly, radiotherapeutic measures demand consideration. In women of 40 or over who are unsuitable for major surgery on account of some coincidental condition such as bronchiectasis, cardiac insufficiency, etc., the use of *x* rays to destroy ovarian activity can be good and satisfactory treatment. On the whole, I prefer this form of radiotherapy to the insertion of radium into the uterine cavity. I have formed this opinion from my experience that intrauterine radium is less certain in its action, which I believe to be essentially destruction of the endometrium, and, moreover, that it may have the distressing sequel of a troublesome and persistent vaginal discharge from the necrosed endometrium. In the younger patient radiotherapy has only the most limited place, if any. Again I could say it is a confession of failure, but it might be used as intrauterine radium in an attempt to produce an effect limited in time and with conservation of the uterus. I have one such case in mind among my own patients, dating back to my early days of practice when hormone treatment was rudimentary. This girl resisted all efforts to control her menorrhagia by drugs: she had intracavity radium, leading to amenorrhoea for some years, but subsequently menstruation returned and she bore a child.

Finally, there is treatment by hormones, and it is here that we have found the Papanicolaou smear of enormous value both in directing and in controlling treatment. I think it is fair to say that often endocrine treatment in functional bleeding has been largely a matter of "by guess and by God," and yet it is a potentially important method of dealing with such cases, especially in adolescents and the younger women in whom radical surgery and radiotherapeutic measures are contraindicated. The work we have been doing is an attempt to get a sound basis for this line of therapy, and also to check the results by the effects reflected in the smears. With this end in view, Dr. Egerton has examined 879 patients and some 2,900 smears. These were by no means all cases of functional bleeding but an effort was made to assess the smears with regard to the value of the picture that they gave of the ovarian function. We now have records of 47 patients whose functional bleeding was treated, and whose treatment was controlled on the evidence provided by vaginal smears. In the menorrhagias of puberty and of the menopause we have found usually low hormonal levels but with relatively high oestrogen production at these low levels. In the early reproductive life there is generally a low hormone level, though not an unbalanced one; and in the later reproductive life an unbalanced hormone production with marked excess of oestrogens. In this way we have had a pointer in selecting the most appropriate hormone to use: sometimes oestrogen, sometimes progesterone, and sometimes both hormones given in cyclical fashion.

This is not the place to discuss in detail the various types of cell found in the smears and on which the diagnosis is based, but the study has been based on the description given by Papanicolaou, Shorr, Bonime, de Allende, and others; and the cornified, precornified, and deep-layer cells described by these workers have been counted and their arrangement has been observed.

Illustrative Cases

When treatment is being undertaken a planned series of smears is used to check the results of therapy cytologically and to compare these results with the effect of the drugs on the symptoms. A brief reference to three cases may help to elucidate the problem.

Case 1.—This patient, aged 14, began to menstruate in April, 1954. The flow was heavy, lasting some seven days, and the intervals were long at first. In August she was referred to hospital because of prolonged menstrual loss, 14–20 days. The endometrium showed no pathological change, but in the smears there was evidence of oestrogen preponderance at low level. Before being referred to hospital this girl was treated by progesterone without effect on the symptoms, but an improvement is being achieved by giving both hormones in cyclical fashion. Our hope is that we shall tide the patient over an interval during which the ovaries will begin to function normally.

Case 2.—A married woman aged 34 came with the complaint of increasing menstrual loss from four days up to twelve or fourteen at regular intervals. She was found to have a generally low hormonal level and was treated with both hormones, given cyclically. In her case the repeat smears were valuable in deciding the amounts to be given. Her cycle became regular and she lapsed in her attendance. After an interval of ten months the symptoms recurred and she returned to hospital. The low hormonal level was again found, and she is again responding to treatment.

Case 3.—A married woman aged 39 came to hospital saying she wished to have a hysterectomy. She gave a history of long heavy periods (14–20 days) at intervals of five to six weeks for five years. Her previous cycle had been 3–4/25–26. She had been given various "pills" and "injections" and had twice been curetted. The endometrium here showed persistent proliferation and the smear an intense oestrogen preponderance with no evidence of progesterone effect. On progesterone therapy the loss has been reduced to normal, but the intervals remain long. In her case I anticipate that treatment is in the nature of replacement therapy and will have to be continued over a prolonged period.

Conclusion

I submit that in cases of functional bleeding the vaginal smear is an important adjunct in diagnosis and a valuable aid in planning and controlling treatment, though it in no way supersedes clinical examination and diagnostic curettage; nor does it exclude surgical treatment, but it does help to place hormone therapy, where indicated, on a rational and controlled basis and so avoids radical surgery in the younger woman with this disabling complaint.

Summary

Functional uterine bleeding is defined as bleeding from the cavity of the uterus for which no cause can be found by general or local clinical examination, or by curettage of the cavity. Post-menopausal bleeding is considered to be of a different character. The diagnosis is made after full physical examination, both general and local, with study of the vaginal smears by the Papanicolaou method, and confirmed by curettage and microscopy of the endometrium. The cases are initially divided into age groups.

Treatment is considered under four headings—symptomatic, surgical, radiotherapeutic, and hormonal—and the indications briefly discussed. The importance of conservative measures in adolescents and in women under the age of 40 is emphasized.

It is claimed that the vaginal smear is a valuable method of assessing ovarian function and of diagnosing variations from the normal, thereby providing a rational basis for hormonal therapy. Such therapy should be controlled by a planned series of smears.

BIBLIOGRAPHY

Bancroft-Livingston, G. (1954). *J. Obstet. Gynaec. Brit. Emp.*, **61**, 628.
Bonime, R. G. (1950). *Amer. J. Obstet. Gynec.*, **60**, 1306.
Mack, H. C. (1953). *J. clin. Endocr.*, **3**, 169.
Papanicolaou, G. N. (1946). *Amer. J. Obstet. Gynec.*, **51**, 316.
—— (1953). Ibid., **51**, 519.
Wachtel, E. (1954). *J. Obstet. Gynaec. Brit. Emp.*, **61**, 155.

CONTRIBUTIONS OF NEURO-ANATOMY AND NEUROPATHOLOGY TO PSYCHIATRY*

BY

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It is sometimes forgotten, amidst the luxuriance of the psycho-analytic jungle, that the roots of our knowledge lie embedded in the soil of the basic sciences. This soil is often alleged to be an extremely inhospitable medium for the growing plant of psychiatry to flourish in, and there has been, particularly in the American continent, such a shift away from these basic sciences as to be quite alarming. It is my contention, and it will be my aim, to show that neuro-anatomy and neuropathology have contributed at least as much as any of the other basic sciences to our present understanding of mental disorder. For such a vast field a review such as this can either be all-embracing and panoramic or, on the other hand, can select certain topics for critical consideration. It is this latter method I have chosen, the topics being schizophrenia, the anatomical problems of leucotomy, the epilepsies, and the senile and presenile dementias.

Before we consider these groups in general, it is proper to consider the techniques which are now available for their investigation. Unfortunately the revolutionary developments in physical science have not, as yet, had their fullest application to anatomy and pathology. The basic methods of microscopical work remain very much unchanged. Sections are stained by a variety of new stains, it is true, but the microscope remains the chief tool. Both anatomy and pathology have, however, become more functional, in the sense that descriptive studies are more and more closely integrated with studies of function. The direction which these two sciences are taking is toward a greater understanding of function in its relation to structure, and as a result there is a considerable use of techniques derived from other fields. Physiological neuronography, for instance, has added a great deal to our knowledge of brain anatomy, whilst histochemistry is developing our understanding of cell structure in terms of biochemistry. It seems proper, therefore, to outline briefly some of these new techniques before passing on to consider the results of their application.

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New Techniques

Of the more orthodox methods, the use of specialized silver impregnation methods has been most rewarding. The advantage of these stains is that the actual axis cylinders, and particularly their terminal arborizations, can be determined, irrespective of the degree of myelinization. M. Meyer (1949), for instance, was able to trace a direct pathway from the dorsal frontal convexity (approximately areas 8 and 6 of Brodmann) to the mammillary bodies and other parts of the posterior hypothalamus. The development of histochemistry will soon have important repercussions in these two sciences. Lison (1936), in France, may be regarded as the first to organize knowledge in this field, and since then there have been rapid advances. A known chemical reaction is used in order to identify substances within a histological preparation, but certain physical properties of substances are also made use of, such as fluorescence, ultra-violet or *x*-ray spectrography, and tracer techniques. The chemical substances in the tissue must first be immobilized in the situations where they occur during life, and the freeze-drying technique has therefore been extensively used. In addition, the chemical reaction or physical method used in order to identify the substances within the section must not interfere with tissue structure, and must produce a reasonably stable result and, preferably, a highly insoluble and deeply coloured precipitate.

In the nervous system enzymatic activity in relation to normal and diseased tissue is clearly an important field for work. Naidoo and Pratt (1954) have traced the development of adenosine 5′-phosphatase activity in the rat cerebral cortex during maturation, and have shown that there is an increase in enzyme activity which is greatest between 15 and 80 days of life. This activity appears to arise in nerve fibres, and may be related to myelinization. They have also (Naidoo and Pratt, 1955) shown that in chickens deficient in vitamin B_1 there is a significant increase in the thiamine pyrophosphatase and alkaline phosphatase activity in the optic tectum, but no change in the acid phosphatase activity. The effects of physical treatments such as leptazol can be investigated experimentally, and the method is full of promise both for neuro-anatomy and for neuropathology.

At the other end there have been advances in microscopy which are perhaps not as well known as they should be. The phase contrast, the reflecting microscope, and the electron microscope have all their individual advantages over orthodox microscopy. To date, however, technical difficulties in dealing with biological specimens have hindered progress, and, to the best of my knowledge, the contributions to our specialty have been negligible.

Schizophrenia

Of the topics which I have chosen for special consideration, that of schizophrenia presents the most difficult problems. In spite of this, anatomical and pathological research into schizophrenia has indirectly opened up new vistas in our understanding of neuro-anatomy. The study of post-leucotomy brains at the Maudsley Hospital by Professor Meyer and his associates has added an impressive chapter

to our knowledge both of the disease and of the human brain. And the work is in many ways still in its infancy. Josephy (1930) reviewed the literature on the histological changes in the brain of schizophrenics, beginning with the communications of Alzheimer (1897, 1913), Buscaino (1920, 1929), and numerous others. The gist of this work was that characteristic changes were found in the brains of schizophrenic patients. These consisted of focal areas of neuronal loss (the so-called *Lückenfelder*), and of a variety of nerve-cell changes in the neurones of the cerebral cortex, ranging from loss of Nissl bodies to alveolar degeneration and fatty degeneration. Buscaino, moreover, described peculiar areas of demyelinization (*zolle di disintegrazione a grappola*) in the white matter of schizophrenic brains, and has up to the present time repeatedly maintained that these are produced by an intoxication. He claims that schizophrenia is the result of an "aminic" toxicosis arising from disorder of the gastro-intestinal tract or the liver.

These findings, however, did not remain unquestioned. Spielmeyer (1930) thought that no characteristic neuropathological changes could be established, and his pupil Peters (1938) published an excellent paper on the subject. By using as control material non-psychotic executed criminals, Peters showed that all the changes which had been described for schizophrenia were also to be seen in his control material. In other words, they were non-specific, and most probably post-mortem artifacts. Wolf and Cowen (1952), using biopsy material, arrived at similar conclusions. However, the controversy has still continued, and in 1952 a symposium was held on the subject at the First International Congress of Neuropathology. Of the seven distinguished workers who delivered communications on this problem, only the voice of Professor Meyer (1952) was raised to point out that there is still no irrefutable evidence of neuropathological change in schizophrenia.

The whole tenor of the communications is that schizophrenia is associated with characteristic changes in the nervous system. The Vogts (1948, 1952), for instance, considered that schizophrenic symptoms were the result of nerve-cell disease, and not the result of loss of nerve cells. By serial sections of the brains of schizophrenics they were able to find a cyto-architectural alteration, with minimal vascular and glial reactions. But, in addition to cortical changes, other parts of the brain are involved. The hypothalamus is always intact, but the medial nucleus of the thalamus is often affected. Anatomically the greatest alterations are in the prefrontal gyrus, the anterior cingular gyrus, the ventral temporal region, and the anterior and mesial nuclei of the thalamus. By a careful clinico-pathological correlation these authors aspire eventually to finding a specific localization for every symptom.

Walter Bruetsch (1952), of Indianapolis, drew attention to the occurrence of rheumatic occlusive endarteritis of the small meningeal and cortical arteries in about 9% of schizophrenic brains. He pointed out that classical cases of schizophrenia, in which no organic disorder has been suspected during life, may on coming to necropsy reveal severe cerebral disease such as diffuse and extensive demyelinization of Schilder type, multiple sclerosis, or brain tumour. The problem of schizophrenia remains, therefore, the problem of establishing various pathological states by new techniques. The fact that in many cases of schizophrenia the brain is normal means only that our techniques are inadequate. "The substratum of schizophrenia," he writes, "is at present too subtle for demonstration by present techniques. The majority of instances of schizophrenia appear to be due to an organic process."

Two-way Approach

These are challenging statements, and demand investigation. Professor Meyer (1952) has approached the problem in two ways. In answer to those who see a specific anatomical localization, he has pointed out that, in all the leucotomized brains of non-schizophrenic subjects with bilateral frontal lobe damage and degeneration of the dorso-medial nucleus of the thalami as a result of the operation, no schizophrenic symptoms have been seen. Nor, indeed, have they been observed with the wide variety of anatomical changes often seen at such operations. Secondly, he carried out a clinico-pathological analysis of 42 cases of "functional psychosis," using both post-mortem and biopsy material. Schizophrenic, depressive, and obsessional patients were all included. Very careful attention was paid to the question of artifact. Meyer remarks, for instance, that the two types of nerve cell which Hyden and Hartelius (1948) regarded as characteristic of schizophrenic brains, and with ultra-violet microscopy as indicative of a lack of nucleotides, can in fact be seen in biopsy specimens from the brains of normal humans and animals. Many of the changes in nerve cells and glia can be correlated with the admission of the two physical treatments—electric shock and insulin coma—whilst the effect of age and systemic disease has also been insufficiently reckoned with. Careful studies such as this are being further implemented at the present time, using a much larger case material and matched controls.

Although neuropathology has on the whole contributed so little to our knowledge of schizophrenia, there is no good reason to despair for the future. For instance, individual cyto-architectonic variations and the maturation processes of the brain in relation to disease have as yet hardly been investigated, whilst neuropathological techniques remain in their infancy. On the other hand, the advance in our knowledge of neuro-anatomy as a result of leucotomy has been astounding. And springing from this knowledge have come the various modifications in neurosurgical procedures.

Anatomical Problems of Leucotomy

In his Henderson lecture, for 1953, Professor Meyer summarized the anatomical results of these operations. The principal afferent fibres passing to the frontal lobes arise in the thalamus, running from the dorso-medial nucleus to areas of granular frontal cortex and from the anterior nucleus to the cingular region. The thalamo-frontal projection is systematically organized—and the thalamic nuclei concerned are in turn linked with the hypothalamus. In animals, fibres passing along the cingular fasciculus connect with the hypothalamus, thus forming a circuit linking frontal lobe, cingular gyrus, and hypothalamus. The afferent projections to Brodmann areas 32 and 12 and to the agranular frontal cortex have not yet been adequately identified, whilst the so-called diffuse thalamic projection system has been the subject of much speculation. Here electro-physiological work on animals has outstripped the work on human material, and still awaits anatomical verification in man.

The facts concerning this diffuse thalamic projection system are of such importance as to require consideration here, in view of the later discussion of the problem of epilepsy. Lorente de Nó (1943) described two types of cortical afferent, one ending in a brush-like arborization in the fourth cortical layer, and the other an "unspecific afferent terminating in all cortical layers, giving rise to many collateral branches. The specific fibres ending in the fourth layer came from the thalamic nuclei, whilst the unspecific ones were either from undetermined regions of the thalamus other than the specific thalamic nuclei, or from transcortical or transcallosal association fibres. At the same time, Morison and Dempsey (1942) were investigating the effect of electrical stimulation of the intralaminar parts of the thalamus, and had observed that cortical electrical activity over a wide area was greatly influenced by stimulation of these areas. Moreover, the effect was quite different from that following stimulation of specific thalamic nuclei. Since then the diffuse thalamic system has attracted great attention, and Jasper (1949, 1954) and Hanbery and Jasper (1953) have demonstrated that, in addition, characteristic wave-and-spike activity of three cycles per second, of the type seen in petit mal, could be evoked from the intralaminar portion of the cat thalamus.

The efferent pathways from the frontal lobe have been more difficult to elucidate, owing to the peculiar fact that retrograde degeneration within the frontal lobe anterior to the leucotomy cut is not usually found. Special silver techniques are therefore needed. However, it has now been established that the frontal lobe sends fibres to the thalamus, hypothalamus, red nucleus, substantia nigra, corpus striatum, corpus luysi, and pons. The ventro-medial nucleus of the thalamus seems to be the most important end-station, and this nucleus, at least in the monkey, also receives fibres from the amygdaloid nucleus and the tip of the temporal pole.

More recently, Elisabeth Beck (1950), who carried out a masterly study of the prefronto-pontine pathway, has shown that a transneuronal degeneration of granular and Purkinje cells occurs in the cerebellum with lesions of the fronto-pontine tract. The long association tracts (superior longitudinal tract, uncinate, angular and subcallosal fasciculi) are also the subject of investigation at the Maudsley Hospital.

These studies in man show that the frontal lobes are connected with thalamus, hypothalamus, and, indirectly, with rhinencephalic centres. They have led to a greater understanding of personality and enabled clinicians to refine their technique. For instance, whilst improvement is related to the amount of white matter involved in the cut, there is some evidence that a regional localization is important in mental functions. Improvement occurs more often with cuts involving the mid-central, orbital, and cingulate sections of white matter than with cuts involving the dorsal and dorso-lateral sectors. With lesions in this latter situation personality changes are often severe. Fulton (1951) has related the effectiveness of orbital and cingulate cuts to involvement of the visceral brain, whilst Professor Meyer (1954) has suggested that owing to the position of the thalamo-frontal projections in these situations it will almost certainly be severed in operations on these areas. Numerous problems of great significance for clinical psychiatry are at last being illumined by facts and not by speculation.

The Epilepsies

Interestingly enough, these anatomical advances have greatly influenced another field of great concern to the psychiatrist. I refer to the problem of epilepsy. Here the combined neuropathological and anatomical investigation of the brain in epileptics has led directly to the relief of suffering. We have seen that anatomical and physiological studies have gone hand in hand, and that the thalamus and basal nuclei have been the main foci of interest. The dramatic effects of stimulation of intralaminar systems in the thalamus on cortical activity, and the production of 3 c./sec. wave-and-spike activity, had immediate repercussions in clinical work on epilepsy. Penfield (1952) had postulated the presence of a centrencephalic system regulating consciousness, and the anatomical data suggested that this might be located in the intralaminar systems of the thalamus, the reticular formation of the brain stem, and the non-specific projection systems.

Anatomical research into this brain-stem system has been carried out by Olszewski and Baxter (1954), whilst the pathological anatomy of epilepsy has been re-examined. For more than a century sclerosis of the cornu ammonis has been recognized in the brains of chronic epileptics. Spielmeyer (1927) noted that it occurred in 80% of 126 epileptic brains which he investigated. He and his pupils, in particular Scholz (1938) and Meyer (1939), have elucidated the pathological changes occurring in epilepsy with great thoroughness.

Marginal sclerosis and Ammon's horn sclerosis, particularly involving the Sommer sector, are common, as is a degeneration of the Purkinje cells of the cerebellum. The cerebral cortex is also affected, particularly the occipital cortex, and then follow the thalamus, dentate, and olives, in order of frequency. These changes are usually slight, but more severe lesions may be seen, and Scholz (1951) has suggested that in some cases of lobar atrophy, or infantile diplegia with epilepsy, the fits may have been responsible for the severe cerebral lesions. The German school has considered, and still believes, that these lesions which I have mentioned are the results of anoxia, and are due to the repeated anoxic insults which occur during recurrent epileptic attacks. The localization of the lesions is related to special factors of vulnerability, such as rates of tissue oxygenation, vascular supply, or susceptibility to the effects of cerebral herniation.

It remained for Penfield, through his work on temporal lobe excision, to bring the whole problem into focus. Penfield and his collaborators (Earle *et al.*, 1953) have suggested that an incisural sclerosis is the commonest cause of temporal lobe epilepsy. It is the result of a herniation of the temporal lobe into the tentorial opening during the head-moulding process of birth. Compression of the anterior choroidal, posterior, and middle cerebral arteries occurs, with a subsequent anoxia. The whole of the temporal lobe may be involved, but the inner and lower parts of the lobe—that is, the uncus and hippocampal gyrus—were most commonly affected. There are, of course, many cases of temporal lobe epilepsy in which a post-natal pathology is found—such as tumours, abscess, or traumatic lesions, but the commonest cause of temporal lobe epilepsy is birth trauma.

This challenging theory of incisural herniation was fundamentally different from that of the German school, which saw the cerebral lesion as the result, and not the cause, of the epileptic attacks. Meyer, Falconer, and Beck (1954) have critically examined both theories on a material consisting of 18 excised temporal lobes. All were cases with a unilateral E.E.G. focus in the temporal lobe and no evidence of a space-occupying lesion. Apart from four cases in which small tumours or post-traumatic lesions were found, the main group of 14 lobes showed a variety of changes ranging from a laminary atrophy of the third cortical layer, or a generalized cortical atrophy, to sclerosis of the cornu ammonis, meningeal fibrosis, marginal glia, and gliosis of the white matter of the lobe. These observations are more in line with the findings and theories propounded by Scholz (1951).

Birth trauma may be one factor, but it certainly is not an exclusive cause of temporal lobe epilepsy, and Meyer, Falconer, and Beck (1954) have put forward convincing reasons for a more comprehensive approach to the problem. In a more recent paper (Meyer and Beck, 1955) he has also drawn attention to the lesions of the amygdaloid nucleus which he has found in certain cases of temporal lobe epilepsy. The anatomical and physiological implications of these findings are of great interest, for the uncus, the amygdaloid, and the transitional cortex of the anterior insula, posterior orbital, and anterior cingular regions make up what the physiologists call the visceral brain. And if it is true that psychiatry is more concerned with feelings than with cognition, then this is the head ganglion, to use Sherrington's words, of the "feeling system."

The Presenile Dementias

Since 1892, when Arnold Pick first described that peculiar disorder of the presenium since named after him, anatomy and pathology have steadily extended our knowledge of these presenile dementias. Inextricably linked with their study is the problem of ageing in general, and the whole field of senile and presenile disease is potentially one of the most fruitful for research. Clinical differentiation, largely as a result of the particular form assumed by the symptoms and signs of these disorders, has only led a certain distance. It has remained for neuropathology to clarify many of the problems. In a sense, it has perhaps been unfortunate that presenile and senile dementias have been associated, for

certainly it is only in Alzheimer's disease and related conditions that the similarity bears examination. The clinical and pathological changes in Alzheimer's disease are identical with those found in the brains both of senile dements and of "normal" old people. But in all the remaining "presenile dementias," to the best of my knowledge, the pathological processes bear no relationship to ageing. The problem therefore has been twofold—the recognition of new clinico-pathological syndromes, and the question of ageing, senile dementia, and Alzheimer's disease.

Even though Alzheimer's and Pick's diseases have been recognized for half a century it is only in the last two decades that serious attempts have been made to differentiate them clinico-pathologically. The neuropathological appearances are characteristic, but, even so, some unusual conditions have come to light during these studies. Worster-Drought *et al.* (1940) described an unusual form of familial presenile dementia associated with spastic paralysis, whilst other authors, from a somewhat different standpoint, had reported similar cases (van Bogaert *et al.*, 1940; Lüers, 1947). In these patients there was an unusual histological picture in that the presence of senile plaques with the neurofibrillary tangles seen in Alzheimer's disease was associated with a change in the media of the blood vessels consisting of a hyalinization and a deposition of amyloid. This change in the blood vessels had already been described by Scholz (1938) in the brains of old people and called by him *drusige Entartung* (plaque-like degeneration). The senile plaques were also unusual in their prominence and their morphology. Divry (1947) had already shown that the central core of many senile plaques with histochemical techniques behaved like amyloid, and that this was also the case with the neurofibrillary tangles. Here, then, was a condition where the changes of Alzheimer's disease were found together with an amyloid change in the blood vessels. Moreover, similar changes occur in the elderly brain. Corsellis and Brierley (1954) have described two further examples of this condition and reviewed the literature. Here is a link between the ageing process and a particular disease which may be of some theoretical importance.

Divry (1947) considers that these amyloid changes represent a change in the physical state of the brain—a colloidal precipitation, with the transformation of a sol to a gel. If this be true, then some of the morphological peculiarities of the senile brain can be better understood; for instance, the different appearances of senile plaques in different sites of the brain.

Jakob–Creutzfeldt Syndrome

There is another group of presenile dementias in which slow but steady progression is being made solely as a result of neuropathological work. Under the name of the Jakob–Creutzfeldt syndrome have been clustered together a heterogeneous collection of disorders. In 1920 Creutzfeldt reported the case of a young woman of 27 dying from a condition characterized by a progressive dementia and signs of bilateral pyramidal disorder. Jakob (1921, 1923) described five cases which he considered essentially similar to the original case of Creutzfeldt. The clinical picture was one of a combination of extrapyramidal, pyramidal, and bulbar or spinal amytrophic signs, together with mental disturbance. Pathologically, degenerative lesions in the nerve cells of the cerebral cortex, basal ganglia, brain stem, and spinal cord were associated with a glial overgrowth in these situations. To such a clinico-pathological syndrome the eponym Jakob–Creutzfeldt has been applied. Twenty-six further cases have since been reported, chiefly in the German literature, and attempts have been made to establish the validity of the syndrome.

Generally speaking, the pathological diagnosis depends more on negative than on positive findings—largely by exclusion of one or other of the well-recognized presenile dementias. What is left is a picture of widespread degenerative change in nerve cells, with a certain degree of systematization. Thus there is a group of cases in which dementia and the signs of motor neurone disease are associated with extrapyramidal features; another in which dementia alone occurs; and a third, recently the subject of a paper by Meyer, Leigh, and Bagg (1954), in which cortical blindness and dementia go hand in hand. The problem is whether in fact these widely varying conditions are members of a homogeneous group, or whether the Jakob–Creutzfeldt syndrome is a hotchpotch of disease, having in common only their relative unclassifiability.

The interesting theoretical status of this alleged syndrome is that the neuronal degeneration and glial overgrowth is also found in most of the senile and presenile dementias, in Huntington's disease, and in most systemic degenerations. It is also encountered in physiological ageing, and Gellerstedt (1933) has pointed out that the larger motor neurones are usually the first to be affected by the ageing process, together with the olives, dentate nuclei, and dorso-medial nucleus of the thalamus. It is in these areas that changes are to be found in cases of Jakob–Creutzfeldt disease. It is tempting to suggest that it represents an exaggerated and premature ageing in wider areas of the central nervous system than is usually involved in system degenerations. The whole question of dementia in such conditions as the hereditary ataxias and cerebellar degenerations is still *sub judice*, and the complex relationships of one disorder to another are still a rewarding field for study.

Conclusions

Nothing is more salutary for the clinician than to review at certain periods of his life the general trends of his specialty. He is often absorbed in clinical work with its loose and humanistic approach, and a reappraisal of the scientific principles on which his work is based is vitally necessary. My own interests have passed through neurology and neuropathology to psychiatry, and in particular to the so-called dynamic psychiatry in relation to psychosomatic medicine. The contributions of anatomy and pathology to psychiatry, as I see it, are of fundamental importance. Psychopathology may be useful for descriptive and perhaps therapeutic purposes, but further advances in understanding will not come other than through the basic sciences. What progress has been made in the past twenty years owes more, I suggest, to anatomy and pathology than to any other of the basic sciences.

Summary

Although technical advances in neuro-anatomy and neuropathology have not kept pace with advances in the physical sciences, a wealth of new information has sprung from these two sciences over the past twenty years. The study of schizophrenia has both directly and indirectly contributed to our knowledge of the anatomy of the brain and of its mechanisms, in health and disease. Although opinions differ, present techniques have not revealed a neuropathology of schizophrenia. Leucotomy, however, has provided a human experiment whereby the relationship of the frontal lobes and basal grey masses has been clarified. Out of this knowledge has developed the concept of the visceral brain, with all its far-reaching implications. Dovetailing with this research, and again largely as a result of neurosurgical work with patients, epilepsy is yielding up some of its mysteries. The temporal lobe is under extensive anatomical scrutiny, as is the neuropathology of epilepsy.

Lastly, neuro-anatomy and neuropathology are seen as playing a more important part in the unravelling of the problems of ageing, and of the presenile dementias. The development of new techniques, particularly histochemical techniques, is full of promise, and already some of the enzymatic processes of nervous tissue have been

elucidated. It is concluded that these two sciences have, in fact, entered upon a new phase of usefulness in the study of psychiatric disorders.

My thanks are due to Professor Alfred Meyer for his continued interest in the problems of a clinician.

BIBLIOGRAPHY

Alzheimer, A. (1897). *Mschr. Psychiat. Neurol.*, **2**, 90.
—— (1913). *Z. ges. Neurol. Psychiat.*, **7**, 621.
Beck, E. (1950). *Brain*, **73**, 368.
Bruetsch, W. L. (1952). *Atti del Primo Congresso Internazionale di Istopatologia de Sistema Nervosa*. **1**, 487.
Buscaino, V. M. (1920). *Riv. patol. nerv. ment.*, **25**, 65.
—— (1929). *Psychiat.-neurol. Wschr.*, **31**, 167.
Corsellis, J. A. N., and Brierley, J. B. (1954). *Brain*, **77**, 571.
Creutzfeldt, H. G. (1921). In Nissl-Alzheimer's *Histologie und Pathologie*, p. 1.
Divry, P. (1947). *J. belge Neurol. Psychiat.*, **47**, 65.
Earle, K. M., Baldwin, M., and Penfield, W. (1953). *Arch. Neurol. Psychiat. (Chicago)*, **69**, 27.
Falconer, M. A. (1954). *British Medical Journal*, **2**, 939.
—— Pond, D. A., Meyer, A., and Woolf, A. L. (1953). *J. Neurol. Neurosurg. Psychiat.*, **16**, 234.
Ferraro, A. (1952). *Atti del Primo Congresso Internazionale di Istopatologia de Sistema Nervosa*, **1**, 630.
Fulton, J. F. (1951). *Frontal Lobotomy and Affective Behaviour*. Chapman and Hall, London.
Gellerstedt, N. (1933). *Upsala LäkFören. Förh.*, **38**, 193.
Gomori, G. (1952). *Microscopic Histochemistry : Principles and Practice*. University of Chicago Press.
Hanbery, J., and Jasper, H. (1953). *J. Neurophysiol.*, **16**, 252.
Hyden, H., and Hartelius, H. (1948). *Acta psychiat. (Kbh.)*, Suppl., 48.
Insua, J. A., and Naidoo, D. (1954). *J. Neurol. Neurosurg. Psychiat.*, **17**, 204.
Jakob, A. (1921). *Z. ges. Neurol. Psychiat.*, **64**, 147.
—— (1923). *Die extrapyramidalen Erkrankungen*. Springer, Berlin.
Jasper, H. (1949). *Electroenceph. clin. Neurophysiol.*, **1**, 405.
—— (1954). *Brain Mechanisms and Consciousness*, p. 374. Blackwell, Oxford.
Josephy, H. (1930). In *Handbuch der Geisteskrankheiten*, edited by O. Bumke, II. Spez. Teil VII, p. 763. Springer, Berlin.
Lison, L. (1936). *Histochemie Animale*. Gauthier-Villars, Paris.
Lorente de Nó, R. (1943). In *Physiology of the Nervous System*, by J. F. Fulton, 2nd ed., p. 274. Oxford.
Lüers, T. (1947). *Arch. Psychiat. Nervenkr.*, **185**, 165.
McLardy, T. (1948). *Brain*, **71**, 290.
—— (1951). *Electroenceph. clin. Neurophysiol.*, **3**, 183.
Meyer, A. (1939). *J. ment. Sci.*, **85**, 927.
—— (1952). *Atti del Primo Congresso Internazionale de Istopatologia de Sistema Nervosa*, **1**, 649.
—— and Beck, E. (1954). *Prefrontal Leucotomy and Related Operations*. Oliver and Boyd, Edinburgh and London.
—— —— (1955). *Proc. roy. Soc. Med.*, **48**, 457.
—— Falconer, M. A., and Beck, E. (1954). *J. Neurol. Neurosurg. Psychiat.*, **17**, 276.
—— Leigh, D., and Bagg, C. E. (1954). Ibid., **17**, 129.
Meyer, M. (1949). *Brain*, **72**, 265.
Morison, R. S., and Dempsey, E. W. (1942). *Amer. J. Physiol.*, **135**, 281.
Naidoo, D., and Pratt, O. E. (1954). *Enzymologia (Amst.)*, **16**, 298.
—— —— (1955). *Biochim. biophys. Acta*, **16**, 75.
Nauta, W. J. H., and Whitlock, D. G. (1954). *Brain Mechanisms and Consciousness*, p. 81. Blackwell, Oxford.
Olszewski, J. (1954). Ibid., p. 54.
—— and Baxter, D. (1954). *The Cyto-Architecture of the Human Brain Stem*. Karger, Basle.
Penfield, W. (1952). *Res. Publ. Ass. nerv. ment. Dis.*, **30**, 513.
Peters, G. (1938). *Z. ges. Neurol. Psychiat.*, **160**, 361.
Scholz, W. (1938). Ibid., **162**, 694.
—— (1951). *Die Krampfschädigungen des Gehirns*. Springer, Berlin.
Spielmeyer, W. (1927). *Z. ges. Neurol. Psychiat.*, **109**, 501.
—— (1930). *J. nerv. ment. Dis.*, **72**, 241.
Van Bogaert, L., Maere, M., and De Smedt, E. (1940). *Mschr. Psychiat. Neurol.*, **102**, 249.
Vogt, C., and Vogt, O. (1948). *Arztl. Forsch.*, **2**, 101.
—— —— (1952). *Atti del Primo Congresso Internazionale di Istopatologia de Sistema Nervosa*, **1**, 517.
Williams, D. (1953). *Brain*, **76**, 50.
Wolf, A., and Cowen, D. (1952). In *The Biology of Mental Health and Disease*, p. 469. P. C. Hoeber, New York.
Worster-Drought, C., Greenfield, J. G., and McMenemy, W. H. (1940). *Brain*, **63**, 237.

The American Embassy in London has issued details of United States pre- and post-doctoral training programmes on the peaceful uses of atomic energy. The courses are open to foreign nationals and last one to two years. The subjects are industrial medicine, industrial hygiene, and radiological physics (radiation protection). Excluding travel, the cost of participation is estimated at a minimum of $2,800 per student for each of the first two courses, and over $4,000 for the last. At present there are no United States funds available to assist foreign students, and it is assumed that the costs will be met by the foreign government or other foreign sponsor. A memorandum giving further details of these courses may be obtained from Mr. P. J. SEARBY, Atomic Energy Office, 1, Richmond Terrace, Whitehall, London, S.W.1.

ANAEMIA OF PREGNANCY IN AFRICANS OF LAGOS

BY

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Severe anaemia is a common complication of pregnancy in all tropical countries (Fairley *et al.*, 1938; Napier, 1940; Russell, 1941). It is one of the most important causes of maternal and infant mortality and one of the most difficult to treat. Experience in Lagos, as elsewhere, has shown that these patients respond poorly to treatment. It has been the custom to put all severely anaemic patients on treatment with iron, liver, and folic acid from the moment they are admitted to hospital rather than wait for the result of blood investigations. Even so, the majority of these patients have shown little response and pregnancy commonly terminates in abortion.

An attempt has been made to investigate these anaemias in some detail, and this paper is a review of 30 patients seen over a period of eighteen months. These were taken at random from the large number of women admitted to hospital for treatment of anaemia. None had had any form of treatment before the first blood and marrow specimens had been examined. Thirteen were subsequently treated with vitamin B_{12}, and their response is described.

Local Geography and Background of Patients

Lagos, the capital of Nigeria, is a busy town and seaport on the coast of West Africa within 10 degrees of the Equator. In this region of high forest, swamps, and lagoons the humidity is high, and although the shade temperature rarely exceeds 90° F. (32.2° C.) the climate is oppressive and encourages a state of torpor in European and African alike.

Though a Yoruba town, Africans of many other tribes are seen, and the population is continually being increased not only by Yorubas from other parts of the western region of Nigeria but also by Ibos from the east and Hausas from the north, attracted to Lagos by the prospect of higher wages. Many of these live in conditions of poor sanitation and gross overcrowding. The cost of living is high, and few Africans can afford the more expensive foodstuffs. Consequently most Southern Nigerians are vegetarian by necessity; meat is too costly to be an important part of their diet. Meals are monotonous and starchy, consisting of stews prepared from cassava, yams, rice, maize, or guinea-corn, with plenty of palm oil or groundnut oil. This may be supplemented with fruit (oranges, bananas, and plantains) and white bread made of high-extraction American flour, which is becoming increasingly popular. Eggs are too expensive and milk is unobtainable.

Apart from the high price of food, many Nigerians (not only those in the poorer sections of the community) will not "waste" money in an attempt to improve their diets, but prefer to spend it on clothing, an important mark of social distinction. The possession of a wife is another indication of prosperity. It is still the custom for the groom to pay his future father-in-law a sum of money, often very considerable, for his bride. This

being so, it is not unusual for a man to start married life in debt, and so be unable to provide for himself, or his wife, or for the family which will shortly arrive.

Procedure

All patients were seen immediately after their admission to hospital. A medical history was obtained and a physical examination made. Blood was removed for a complete cell count, including a reticulocyte count, and calculation of the standard indices. The figures quoted in this paper for the mean corpuscular volumes have all been subjected to correction for reticulocytosis (Foy *et al.*, 1950). The haemoglobin concentration was determined by conversion to alkaline haematin and comparison with Harrison and Gibson's artificial standard in an EEL photoelectric colorimeter. (The standard itself was checked against a freshly prepared solution of alkaline haemin.) The red cells were examined for the sickle-cell trait, and thick films were examined for malaria parasites.

Sternal puncture was performed, the marrow fragments being separated from the aspirated material and smears made. In 27 cases sufficient blood was obtained for the estimation of total and differential serum proteins and for direct and indirect van den Bergh tests. Specimens of stool and urine were examined for blood and parasites in 24 patients. Gastric analysis was done in only three.

Although it is desirable to do daily reticulocyte counts for as long as a week before the onset of treatment, this was not permissible in any of the patients in this series. The severity of the anaemia and the risk of abortion demanded immediate treatment. After the first dose of vitamin B_{12} reticulocyte counts were done every alternate day, and the haemoglobin concentration and number of red cells were estimated at weekly intervals. None of the patients had any form of dietary control; meals were provided by friends and relations, who visited the hospital daily.

A complete follow-up of patients was found to be impossible. Such is the congestion at the maternity hospital that patients are discharged as soon as their haemoglobin concentration has reached a level of 50–60%, with instructions to attend the out-patient department for continued treatment; others discharged themselves against advice. Many fail to reappear after they have left the hospital. Only three of the patients in this series consented to visit the pathological laboratory for weekly blood examinations.

The criteria used in this investigation as evidence of a deficiency of haemopoietic liver principle are (*a*) the presence in either the marrow or peripheral blood of abnormal white cells (giant stab cells or metamyelocytes, giant multi-segmented polymorphs) and/or (*b*) the presence in the marrow of typical Ehrlich megaloblasts or intermediate megaloblasts (Zuelzer *et al.*, 1947; Dacie and White, 1949).

Clinical Features

Twelve of the women were primiparae. Nine were seen within the first week after delivery, and the remainder (with two exceptions) were seen during the second half of pregnancy.

Although many of the women were profoundly anaemic their symptoms were rarely sufficient to cause them grave inconvenience. Few complained of any more than increasing weakness and lethargy, dyspnoea on exertion, or dizziness and fainting. One girl presented herself at the out-patient department, having walked unaccompanied to the hospital, with a red-cell count of 915,000 per c.mm. and a haemoglobin concentration of 3.2 g.%; she would admit to no symptoms other than those of pregnancy.

Five of the patients showed poor physical development, two of whom had mild oedema which could not be attributed to either the pregnancy or renal or cardiac disease. None of the patients had soreness of the tongue or mouth, and none had skin lesions suggestive of poor nutrition. There was palpable enlargement of the liver in 13 patients and of the spleen in 18 (including all of those with large livers). Five women were clinically jaundiced. Low-grade fever was present in 10 patients, all of whom had either a urinary or an upper respiratory tract infection.

Laboratory Findings

Haematology

The red-cell counts when first examined were below 1 million in 5 cases, 1–2 millions in 17 cases, 2–3 millions in 5 cases, and over 3 millions in 3 cases (range 0.69–3.4 millions per c.mm.). The haemoglobin concentrations varied between 2.5 and 11 g.%. The range of mean corpuscular volumes and the distribution of cases according to cell size are shown in Table I. The high incidence of macrocytic anaemias is well demonstrated, and there would seem to be a tendency towards macrocytosis even when the M.C.V. falls in the normal range of 82–95 cubic microns.

TABLE I.—*Mean Corpuscular Volume* (*Range:* 69–132 *cubic microns*)

	Microcytic M.C.V. Below 82	Normocytic		Macrocytic M.C.V. Over 95
		M.C.V. 82–88	M.C.V. 89–95	
No. of cases seen..	2	2	6	20
No. of cases with evidence of deficiency of haemopoietic principle	1	0	4	15

Although 13 cases were hyperchromic as shown by their colour indices and mean corpuscular haemoglobins, only five had a mean corpuscular haemoglobin concentration in the normal range of 32–38%. The majority of these patients, therefore, were iron-deficient, or were liable to become so in the event of a rapid response to treatment. The mean corpuscular haemoglobin concentrations were below 20% in 1 case, 20–25% in 2 cases, 25–32% in 22 cases, and over 32% in 5 cases (range, 18.5–35%).

The mean corpuscular diameter was measured in only seven cases, all of them macrocytic, as shown by the M.C.V. In all of these the M.C.D. was greater than 7.7 microns, the upper limit of normal (Whitby and Britton, 1953), and the range was 7.8–9.3 microns.

The leucocyte counts varied between 4,300 and 19,600 per c.mm., and were below 5,000 in 2 cases, 5,000–8,000 in 9 cases, 8,000–12,000 in 10 cases, and over 12,000 in 9 cases. In all cases neutrophil polymorphs were the predominant cells. There appears to have been no depression of the myeloid series as was described by Woodruff (1951) in his series of cases seen at Ibadan.

The sickle-cell trait was present in 4 of the 30 patients. One other (Case 5) showed marked sickling of her red cells, with large numbers of bizarre filamentous forms. She became deeply jaundiced after delivery of a live child (which died, however, within a few hours of birth), and she died without showing a response to any form of treatment. It is probable that she had sickle-cell anaemia, but this was not confirmed.

Malaria parasites were found in only one patient; another carried microfilaria of *Loa loa*.

Marrow Examinations.—In almost every patient the marrow was highly cellular, the appearance being one of hyperplasia of both red- and white-cell series with erythroblasts often predominating. The myeloid:erythroid ratios varied between 3.5:1 and 1:3.0. There appeared to be no relationship between the severity of the anaemia and the cellularity of the marrow. Seven patients had typical Ehrlich megaloblasts, six had intermediate megaloblasts, and seven others had abnormal white cells only. Thus 20 patients had evidence of a deficiency of the liver haemopoietic principle; of these, 15 had macrocytic anaemias, four were normocytic (all in the upper range of normal), and one had a microcytic anaemia. Apart from intermediate megaloblasts in her marrow this last patient (Case 13) had numerous giant stab cells and metamyelocytes and multi-segmented polycytes in both peripheral blood and marrow (Tables I and II).

TABLE II.—*Distribution of Cases with Megaloblasts and Abnormal White Cells*

Cell Type	M.C.V. (Cubic Microns)		
	Below 82	82–95	Over 95
Abnormal white cells only	0	1	6
Intermediate megaloblasts	1	2	3
Ehrlich megaloblasts ..	0	1	6

Biochemistry

Total and differential serum proteins were estimated in 27 patients, and the figures agree well with those of Woodruff (1951), using the same normal values: total serum protein, 5.6–8.5 g.%; albumin, 3.4–6.7 g.%; globulin, 1.2–2.9 g.%; albumin/globulin ratio, 4/1–1.2/1. The total protein values were within normal limits in 22 patients, although half of these were approaching the lower limit of normality. Four patients had values below normal, and one above (range, 5.2–9 g.%). The albumin was low in 16 patients (range, 1.5–4.5 g.%) and the globulin raised in 24 (range, 1.7–5.4 g.%). Only six patients had normal albumin/globulin ratios (range, 2.65/1–1/2.65). No account has been taken of the hydraemia which normally occurs during pregnancy, but this would not be sufficient to account for the degree of abnormality of these figures or for the reversal of the albumin/globulin ratios. Similar figures have been found in other Africans admitted to hospital for investigation of anaemia (males and non-pregnant females) and in those in whom marked fatty degeneration of the liver was demonstrated at necropsy. Woodruff (1951) also found that many of his patients had livers fibrosed or infiltrated with fat. Low albumin and high globulin levels have been described in patients with liver disease (Maizels, 1946), and it is thought that this may be an explanation of the abnormal protein levels in the patients of this series. It is believed that the protein-deficient diets of the local Africans are an important factor in the aetiology of this condition.

The van den Bergh test was done on specimens of blood from the same 27 patients. The bilirubin was raised above 0.8 mg. per 100 ml. (the upper limit of normal) in seven patients, the highest reading being 4 mg. per 100 ml.

Fractional Test Meal

This test was done in only three of the megaloblastic patients. Two had normal acid curves, and the third (Case 21) had a histamine-alcohol-fast achlorhydria. As this patient's condition improved, however, her free gastric acid returned and she eventually had an acid curve well within normal limits.

Stool Examinations

Specimens of stool were examined (by the routine direct wet film method and also by a simple concentration technique) from 24 patients: ova of *Ascaris lumbricoides* were present in 12, *Trichuris trichuria* in 9, and *Ancylostoma duodenale* in 11. Both free and encysted forms of *Entamoeba histolytica* were present in one patient.

Response to Treatment with Vitamin B_{12}

Thirteen patients were treated with vitamin B_{12} and iron, nine during pregnancy and four immediately after delivery. The dosage of vitamin B_{12} ("cytamen") used depended on the severity of the anaemia and the response following the first injection. In most cases 100 or 200 μg. was given initially, followed by 20 or 50 μg. at weekly intervals. These patients responded as follows:

Patients Treated After Delivery

Two patients did not respond to vitamin B_{12} or to any other treatment. The first of these (Case 5) had a reticulocytosis from 3.2 to 32.3% after six days, but then became deeply jaundiced and died 13 days after the onset of treatment. As mentioned previously, sickle-cell anaemia with a haemolytic crisis was probably the true diagnosis in this case. The second (Case 19) had a very hypoplastic marrow with no evidence of active erythropoiesis, and died two weeks after admission to hospital.

Case 20 (R.B.C., 1,370,000 per c.mm.; Hb, 4.2 g.%; M.C.V., 105.4 cubic microns) had a macronormoblastic marrow with large numbers of abnormal leucocytes. She was given 200 μg. of vitamin B_{12}, followed by 50 μg. weekly. Her reticulocytes rose to a maximum of 14% on the seventh day. On the seventeenth day the red-cell count was 3,400,000 and the Hb 8.4 g.%. She was discharged one month after the onset of treatment, when the blood count was 4,000,000 and Hb 9.4 g.%.

Case 23 (R.B.C., 1,500,000; Hb, 3.6 g.%; M.C.V., 100 cubic microns) showed intermediate megaloblasts and abnormal leucocytes in her marrow. She received 200 μg. of vitamin B_{12} followed by 20 μg. weekly, and the reticulocytes rose from 4.8 to 11.8% after seven days. After 14 days the Hb concentration had more than doubled (to 8.6 g.%) and the red-cell count had risen to 2,810,000. Seven days later she was discharged, the red-cell count then being 3,100,000 and Hb 9.5 g.%.

Although these last two patients appeared to respond well to vitamin B_{12}, the response coinciding with the beginning of treatment, it is not possible to exclude a spontaneous recovery following the termination of pregnancy.

Patients Treated During Pregnancy

Case 6 (R.B.C., 915,000; Hb, 3.2 g.%; M.C.V., 120 cubic microns) showed megaloblastic erythropoiesis and abnormal leucocytes. She was given 100 μg. of vitamin B_{12} followed by 20 μg. weekly, and her reticulocytes rose from 1.8 to 14% in 11 days. After six days the red-cell count had risen to 1,700,000 and the Hb to 4.7 g.%. She was discharged 13 days after the commencement of treatment, when the Hb was 7.7 g.%.

Case 8 (R.B.C., 1,490,000; Hb, 5.4 g.%; M.C.V., 116 cubic microns) had macronormoblastic erythropoiesis with abnormal leucocytes. She received the same treatment as Case 6 but iron was withheld. The reticulocyte count rose from 8.4 to 14% in eight days, and five days after the first injection the red-cell count had become 2,130,000; the Hb, however, had fallen to 4.9 g.%. She was then given "ferrivenin" (5 ml. on alternate days); six days later she was discharged from hospital with a red-cell count of 2,870,000 and Hb 7.7 g.%.

Case 12 (R.B.C., 1,060,000; Hb, 3.6 g.%; M.C.V., 113 cubic microns) had megaloblastic erythropoiesis and abnormal leucocytes. She was given the same treatment as Case 6, and her reticulocytes rose from 2.4 to 16% in nine days. On the fourth day the red-cell count was 1,830,000 and the Hb 5.6 g.%. Five days later the Hb was 6 g.%, and 15 days after the beginning of treatment she was discharged with an Hb concentration of 8 g.%.

Case 18 (R.B.C., 880,000; Hb, 2.5 g.%; M.C.V., 91 cubic microns) showed megaloblastic erythropoiesis with large numbers of abnormal leucocytes. She received 200 μg. of vitamin B_{12}, and as the response appeared to be slow this was followed by another 200 μg. one week later; she had two further injections of 100 μg., each at weekly intervals. After 10 days the Hb concentration had only reached 3.8 g.%. Eight days later the red-cell count was 2,230,000 and the Hb 5.3 g.%. Twenty-four days after the onset of treatment the Hb was 7.3 g.% and the patient was discharged.

Case 21 (R.B.C., 1,270,000; Hb, 3.4 g.%; M.C.V., 101 cubic microns) had megaloblastic erythropoiesis and abnormal leucocytes. There was a histamine-alcohol-fast achlorhydria. She was treated with folic acid, to which she showed no response. (She received a total dosage of 140 mg. of folic acid, administered over seven days. At the end of this time the Hb concentration was 3.1 g.%.) The folic acid was discontinued and she was given 100 μg. of vitamin B_{12}. This was repeated after one week, and subsequently she was given 50 μg. weekly. The reticulocyte count was high when she was first seen (10%). After an initial rise to 16% it slowly fell and at the end of the second week it was 1.4%. Her blood counts improved as follows: Original count: R.B.C., 1,270,000; Hb, 3.4 g.%. One week after folic acid: Hb, 3.1 g.%. Six days after vitamin B_{12}: R.B.C., 1,580,000; Hb, 5 g.%. After 10 days: R.B.C., 2,220,000; Hb, 6.3 g.%. After 21 days: R.B.C., 2,430,000; Hb, 7.5 g.%. After four weeks: R.B.C., 3,000,000; Hb, 8.8 g.%.

There was no further improvement, and she was discharged. She was delivered of a live child 11 days after the last blood count. This patient had been deeply jaundiced, with a palpable liver and spleen, when she was first examined. The jaundice slowly disappeared and the serum bilirubin was normal when she reached full term. It may be that the slow improvement was largely due to the termination of the haemolytic process. The marrow was examined again before she was discharged and was then normoblastic. Fractional test meal was repeated and showed normal gastric acid production.

Case 24 (R.B.C., 1,700,000; Hb, 4.2 g.%; M.C.V., 88 cubic microns) had intermediate megaloblasts and abnormal leucocytes in the marrow. She was given 200 μg. of vitamin B_{12} followed by 50 μg. weekly. The reticulocytes rose from 3.4 to 18.6% after 10 days. One week after the commencement of treatment the red-cell count had risen to 2,230,000 and the Hb was 5.5 g.%. She was discharged six days later, when the red-cell count was 3,040,000 and Hb 7.1 g.%.

Case 25 (R.B.C., 1,000,000; Hb, 2.5 g.%; M.C.V., 132 cubic microns) had a hypocellular marrow with megaloblastic erythropoiesis. She was given 100 μg. of vitamin B_{12} daily for three days, followed by 100 μg. weekly. The reticulocytes rose from 7.6 to 16.4%, but this was not followed by any improvement of the anaemia. Six days later the red-cell count had fallen to 730,000 and the Hb was 2.3 g.%. In addition to the vitamin B_{12} she was given liver and folic acid, but there was still no response, and she aborted five days later. She continued on the same treatment and slowly recovered over a course of many weeks.

Case 29 (R.B.C., 3,400,000; Hb, 11 g.%; M.C.V., 96 cubic microns), although only mildly anaemic, was macrocytic and had intermediate megaloblasts in the marrow. Treatment brought about a reversion to normoblastic erythropoiesis, but there was little change in the blood picture. (The Hb concentration reached 11.9 g.% and then remained stationary.)

Case 30 (R.B.C., 2,200,000; Hb, 6.8 g.%; M.C.V., 100 cubic microns) showed megaloblastic erythropoiesis with abnormal leucocytes. She had one injection of 200 μg. of vitamin B_{12}. The reticulocytes were 10% on admission to hospital and remained at this level. Seven days later her Hb concentration was 8.3 g.%. Unfortunately she then left the hospital against advice before any further red-cell counts were done.

Discussion

The cases described demonstrate the high incidence of macrocytic anaemias in pregnant women admitted to hospital in Lagos. The M.C.D. was calculated (and found to be increased) in only seven cases, but it has been assumed that the high M.C.V. in other cases does in fact represent an increase in cell diameter; this assumption was substantiated by the appearance of the red cells in the stained film. Woodruff (1951) commented that this increase in cell diameter was present in many anaemias which would be classified as microcytic or normocytic if judged by the M.C.V. alone, and concluded that there must be a diminution in cell thickness in these cases. In the patients described here the increase in cell volume was not accompanied by a corresponding increase in haemoglobin content, and most of the women were hypochromic.

Also outstanding was the high proportion of patients who were shown to be deficient in the liver haemopoietic principle; their anaemias might be classified as being nutritional, although they were not necessarily macrocytic. The occurrence of megaloblastic erythropoiesis in patients with microcytic or normocytic anaemias was observed by Foy *et al.* (1952) in East African patients.

The high incidence of abnormal serum protein values agrees with the findings of Woodruff (1951). Similarly, evidence of a haemolytic process, commonly found in these patients, has been reported before (Fairley *et al.*, 1938; Foy *et al.*, 1950, 1952; Woodruff, 1951). Whether these haemolytic anaemias are secondary to hypersplenism, a sequel of liver damage, or whether they are a result of chronic malaria has still to be decided. Foy *et al.* (1952) believe that "any factor that predisposes the individual to enlargement of the spleen may lead to the development of this splenic haemolytic anaemia," and they suggest that schistosomiasis may play a part in the aetiology of this condition. In Southern Nigeria, however, schistosomiasis is not commonly seen, and malaria (which is highly endemic in this region) is probably a more important factor. Whatever the cause of this haemolytic type of anaemia in pregnant women it seems unlikely that either malaria or worm infestations do more than add to the patient's burden: they aggravate an anaemia which is already present, and which is primarily nutritional in origin, and they hinder the patient's recovery.

The precise nature of the deficiency in these cases is still a matter of some doubt. It is generally believed that the megaloblastic pregnancy anaemias seen in temperate climates and those seen in the Tropics are not identical in aetiology. The former respond well to treatment with folic acid, and it is thought that they may be due to a state of folic acid deficiency (Thompson and Ungley, 1951), possibly a result of a temporary inability either to store or to mobilize it from the liver. Similar anaemias in the Tropics will not respond to folic acid, however, and it has been stated that their response to any form of treatment before parturition is disappointing, and that in most cases it is only possible to arrest the progress of the anaemia (Napier, 1940; Woodruff, 1951). Patel and Kocher (1950) reported five cases of megaloblastic anaemia of pregnancy in Indians, all of which were treated with vitamin B_{12} alone (four had 40 μg. and one had 20 μg.), and all responded. No such response was observed in Woodruff's patients at Ibadan.

In the present series nine patients were treated before parturition, the doses of vitamin B_{12} used being larger than those used by previous workers. Seven patients responded to treatment, four of them rapidly and three more slowly. In all of these the clinical improvement was striking; six were discharged with instructions to attend the out-patient department for further supervision, and the seventh felt so well one week after the first injection of vitamin B_{12} that she discharged herself. Unfortunately, only three patients were followed up for any length of time, and they showed no further improvement after the haemoglobin concentration had reached a level of 8–9 g.%. These results appear to be very similar to those described by Das Gupta *et al.* (1953) in Indian patients with nutritional macrocytic anaemia who were treated with vitamin B_{12}. Although all of their 22 patients showed a good initial response, in only five was there complete remission. The remainder needed crude liver or folic acid to effect recovery. It seems possible that the patients described in this paper might have responded further had folic acid been given at the stage when vitamin B_{12} ceased to be effective.

The lack of response to folic acid of pregnancy anaemias in African women does not necessarily imply that these cases differ in aetiology from those seen in temperate climates. It is obvious that there must be a multiple deficiency, and that complete recovery cannot be expected to follow the use of only one of the many haemopoietic factors. It may well be that the primary aetiology is the same in all patients, whether African or European—that is, a temporary deficiency of folic acid brought about by a metabolic upset which is precipitated by the stresses of pregnancy. In the African this upset is augmented by the presence of liver disease, while parasites in the blood or in the intestines add to the severity of the anaemia. It is possible that the African woman will not respond to folic acid, however, until the secondary deficiency of extrinsic factor has been corrected. Presumably this is brought about by vitamin B_{12}, and the lack of response beyond a certain level coincides with the depletion of the already low reserves of folic acid. The deficiency of extrinsic factor may be the result of a change in intestinal flora which is encouraged by the high-carbohydrate and low-protein diet. After parturition, though there may be a slow spontaneous recovery as folic acid again becomes available, the secondary deficiency persists, and vitamin B_{12} given to these patients will lead to a more rapid recovery.

Summary

Severe anaemia is commonly seen in pregnant women in Lagos. It is an important cause of maternal mortality, and the risk of abortion in these cases is very great. Thirty patients have been investigated and 13 of them were treated with vitamin B_{12}. The clinical and laboratory findings are described, and the response to treatment is discussed with reference to the aetiology of the anaemia. The following conclusions have been reached.

1. Most of the anaemias are macrocytic and hypochromic, and the incidence of nutritional anaemias, diagnosed by the presence of Ehrlich or intermediate megaloblasts and/or abnormal white cells, is higher than has generally been supposed.

2. Many cases are complicated by disease of the liver and by the presence of parasites in the blood or intestines. These add to the severity of the anaemia, and they may be important as causes of hypersplenism and the resulting haemolytic type of anaemia.

3. All patients should be treated with iron, and many will respond to vitamin B_{12} in doses of 100–200 μg. Folic acid may be necessary in addition for complete remission of the anaemia.

4. It is suggested that there is a multiple deficiency in these patients. Although in all pregnancy megaloblastic anaemias the primary defect may be the non-availability of folic acid, the local Africans have in addition a deficiency of extrinsic factor and will not respond to folic acid until this has been corrected.

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References

Dacie, J. V., and White, J. C. (1949). *J. clin. Path.*, **2**, 1.
Das Gupta, C. R., Chatterjea, J. B., and Basu, P. (1953). *British Medical Journal*, **2**, 645.
Fairley, N. H., Bromfield, R. J., Foy, H., and Kondi, A. (1938). *Trans. roy. Soc. trop. Med. Hyg.*, **32**, 132.
Foy, H., Kondi, A., and Hargreaves, A. (1952). Ibid., **46**, 327.
—— —— —— and Lowry, J. (1950). Ibid., **43**, 635.
Maizels, M. (1946). *Lancet*, **2**, 451.
Napier, L. E. (1940). *Indian J. med. Res.*, **27**, 1009.
Patel, J. C., and Kocher, B. R. (1950). *British Medical Journal*, **1**, 924.
Russell, B. A. S. (1941). *Lancet*, **2**, 792.
Thompson, R. B., and Ungley, C. C. (1951). *Quart. J. Med.*, **20**, 187.
Whitby, L. E. H., and Britton, C. J. C. (1953). *Disorders of the Blood*. Churchill, London.
Woodruff, A. W. (1951). *British Medical Journal*, **2**, 1415.
Zuelzer, W. W., Newhall, A., and Hutaff, L. (1947). *J. Lab. clin. Med.*, **32**, 1217.

DIVERGING SEX-MORBIDITY TRENDS IN CANCER OF THE MOUTH

A HOSPITAL MORBIDITY STUDY

BY

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A salient feature of the total incidence of cancer is its apparent uniformity after cognizance has been taken of such influences as improved diagnostic facilities and the ageing population. Despite this overall consistency, gradual changes do occur in morbidity and mortality patterns for specific anatomical sites. An obvious and widely publicized example is the continuing increase in cancer of the lung.

Another progressive trend which has engendered comment is the apparent decrease in cancer of the mouth suggested by a falling standardized mortality rate for both sexes beginning in the later part of the decade 1930–9 (Registrar-General, 1947). That the observed decrease was not entirely attributable to a higher success rate in treatment was confirmed by hospital statistics (Paterson, Tod, and Russell, 1946, 1950). The inference from mortality statistics is that the decrease applies to both sexes (Registrar-General, 1953; Minister of Health, 1954).

The object of this survey is to show that in the North-west of England, over an interval of a decade, there is evidence of a marked decrease in the incidence of cancer of the mouth in men only, a trend which is not apparently common to the adjacent anterior and posterior sites of lip and pharynx. In women, on the contrary, there is evidence of an increase in the morbidity rate, and it seems feasible that the falling mortality rate may be accounted for by their better response to treatment (Russell, 1954).

Basis of the Survey

The data used are culled from the individual statistical abstracts of cases of previously untreated or "new" cancer of the mouth registered at the Christie Hospital and Holt Radium Institute and its peripheral clinics in the North-west of England during the periods 1935–9 and 1945–9. After the inception of the National Health Service in July, 1948, and the establishment of regional hospital board areas, three clinics were ceded to the Liverpool Region. For the purpose of ensuring comparability, therefore, all registrations of patients from the affected territory have been excluded from both series.

The map printed overleaf shows the Manchester R.H.B. area and the location of the peripheral clinics held regularly by consultants from the Christie Hospital and Holt Radium Institute. Some of these clinics were established over twenty years ago and had steadily expanded as their advantages became obvious. Detailed investigation of registrations in each separate clinic area indicates that it is valid to use for comparison in the two five-year periods registrations from all the remaining area with the exception of the shaded part of East Lancashire, which was not served by the Christie Hospital and Holt Radium Institute in 1935–9, although it was subsequently. The analyses in both periods relate, therefore, to patients residing in the area left unshaded on the map.

Table I.—*Populations in Surveyed Parts of Manchester R.H.B. Area*

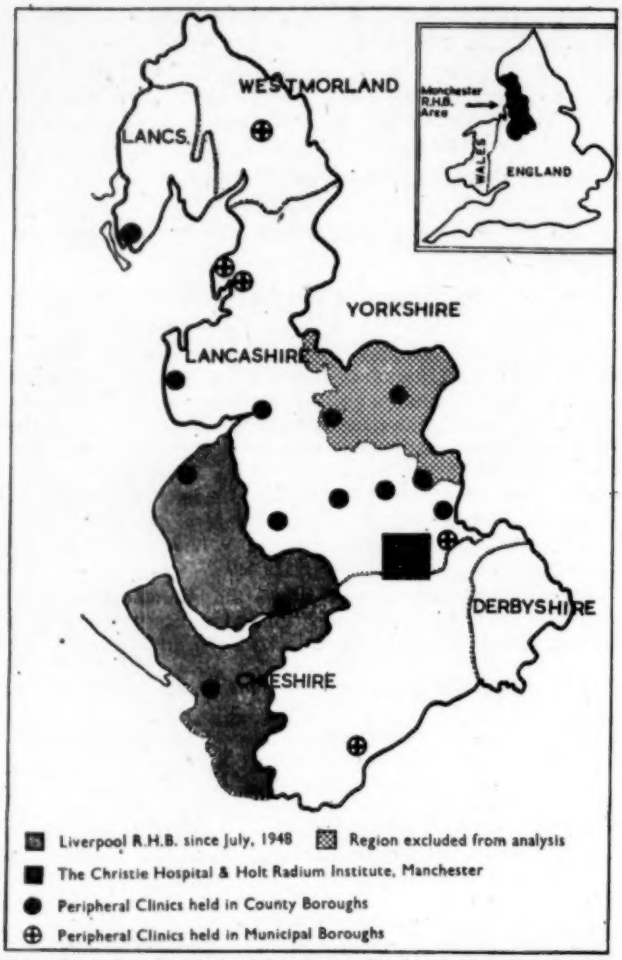
Local Authority	Mid-Year Estimates	
	1937	1947
County boroughs	1,816,220	1,747,970
Municipal boroughs and urban districts ..	1,523,088	1,592,319
Rural districts	257,856	271,878
Total	3,597,164	3,612,167

The whole R.H.B. territory is nearly 3,000 square miles in extent, and the population is approximately 4½ million (47% men, 53% women). South Lancashire is the most heavily industrialized community in the world; consequently the average density of the population in the R.H.B. area is 2.6 persons per acre, compared with 1.2 for England and Wales. Although the area is only one-twentieth the size of England and Wales, it contains one-tenth of the population. Immigration of other races has been of too recent development to have any influence on the investigation.

Table I gives the population in 1937 and 1947—the mid-year of the periods 1935–9 and 1945–9—for the unshaded part of the map according to the type of local authority. These figures have been compiled from the mid-year estimates of the Registrar-General (1938 and 1949) for individual county and municipal boroughs, urban and rural districts.

Criteria of Classification

In the analyses individual cases have been classified according to the site in which the primary lesion was believed to originate. They are shown in three main groups: (*a*) tongue; (*b*) main oral cavity—that is, the anterior part, comprising the upper and lower alveoli, cheek, hard palate, and floor; and (*c*) faucial region (or posterior oral cavity),



The surveyed part of the Manchester Regional Hospital Board area (unshaded).

which includes the soft palate, anterior pillar of fauces, and tonsil. This classification does not exactly conform to the International List definitions of the mouth, Nos. 140–4, but is regarded as preferable for some purposes, since the fusing of hard and soft palate into one group conceals certain characteristics (Russell, 1954).

Tumours of the salivary glands are not included in the survey. Many cases of "mixed salivary tumours" are dealt with by surgeons in other hospitals in the area, and the records of the Christie Hospital and Holt Radium Institute are therefore not as reliable an index to morbidity as is the case with carcinoma of the mouth, for which the treatment policy in the North-west is almost exclusively radiotherapy.

Trends in Hospital Registrations

Table II shows the number of new patients with cancer of the mouth for 1935–9 and 1945–9. The difference in total registrations for men represents a decrease of 28% over the decade; corresponding figures for women amount to 76% increase.

TABLE II.—*Cancer of the Mouth.* Number of New Patients from Surveyed Area Registered at the Christie Hospital and Holt Radium Institute*

Classification	Males		Females	
	1935–9	1945–9	1935–9	1945–9
Tongue	382	302	46	99
Main oral cavity	370	266	61	93
Faucial region	325	209	12	17
Total	1,077	777	119	209

* Excludes salivary gland tumours, totalling 72 in 1935–9 and 89 in 1945–9.

In comparison, for the adjoining anterior and posterior sites of lip and pharynx, upward trends amounting to 39% and 40% respectively for males have occurred. The incidence of cancer of the lip is virtually negligible in females; for cancer of the pharynx there was an increase of 103%. Some of the increase in lip and pharynx registrations is doubtless accounted for by a higher proportion of patients having been directed to hospital than had hitherto been the case. Nevertheless, it seems feasible that this rather high increase also indicates a genuine rise in incidence in both sexes, and that in males the downward trend is confined to the tongue and mouth.

Trends in Morbidity Rates at all Ages

Hospital registrations cannot, of course, be interpreted as a reliable index to morbidity unless they are believed to be an adequate representation of total morbidity and can be related to a defined population. As an essential prerequisite of the survey, measures were adopted to try to ensure that both criteria are complied with. Table III therefore shows the conversion into morbidity rates, expressed as per million living persons at all ages in the area at risk to develop cancer of the mouth. In view of the altered age-constitution of the population within a decade, crude rates are fallacious for purposes of comparison. Accordingly the 1945–9 rates for each sex have been standardized to the same age-distribution as 1935–9.

The extent of the changes in morbidity rates is expressed in percentage form in Table IV. Rounding off of decimal places to the nearest whole digit in Table III is responsible for any disparity observed between these figures and the actual percentage changes shown in Table IV.

TABLE III.—*Trends in Morbidity Rates (5-Year Average Annual Registrations Expressed as Per Million Population at All Ages)*

Classification	Males		Females	
	1935–9 (Crude)	1945–9 (Standardized to 1935–9)	1935–9 (Crude)	1945–9 (Standardized to 1935–9)
Tongue	45	28	5	8
Main oral cavity	44	25	6	8
Faucial region	38	19	1	2
Total	127	72	12	18

TABLE IV.—*Changes in Morbidity Rates for Each Sex Over a Decade*

Classification	Percentage Difference	
	Males	Females
Tongue	−38%	+60%
Main oral cavity	−43%	+33%
Faucial region	−50%	+(100%)
Total	−43%	+42%

Brackets denote that the enclosed percentage is based on a low incidence.

It is interesting to note that for all sites in the mouth the decrease for males is 43%, whereas the increase for females amounts to the almost identical figure of 42%. In the separate main sites the greatest morbidity decrease of 50% for males has occurred in the faucial region. The female morbidity rate in the same site is too low for the 100% increase to have any significance. The most striking change for females is the 60% increase in cancer of the tongue.

Change in Sex Ratio

The divergence in morbidity trends alters the sex ratio to a considerable extent. In Table V the ratios in the two periods, expressed as males to 100 females, are shown on a standardized basis. It will be seen that the ratio male to female has more than halved over the decade, and that the difference is greatest in the tongue group.

Although the sex ratio for the tongue differs appreciably from the male to female figure of 1.6 : 1 given by Mackay

TABLE V.—*Changes in Sex Ratio Over a Decade*

Classification	Standardized Ratio—Males to 1 Female	
	1935–9	1945–9
Tongue	10·0	4·1
Main oral cavity	7·5	3·7
Faucial region	34·8	16·3
Total	11·1	4·9

(1951), the series from which the latter ratio derives is restricted to in-patients, and as a higher proportion of men suffer local recurrence or dissemination of the disease (Russell, 1954), often necessitating readmission to hospital, such a disparity is not unexpected.

Age-Specific Morbidity Trends

Cancer of the mouth remains of comparatively low incidence in the community until the sixth decade of life—a fact which is not, of course, reflected in the formal mode of expression of the morbidity rate at all ages. For the purpose of studying the changing morbidity pattern in greater detail, therefore, it is necessary to investigate the age factor.

The ages used for analysis are those recorded at the time of hospital registration. In some sites, where clinical symptoms may be of long duration, it would obviously be preferable to use the age at the stated onset. In cancer of the mouth, however, such an adjustment to the registration age groups would be very slight, since only about 10% of patients may be expected to report symptoms exceeding one year in duration.

In Table VI the age-specific trends for each decennial group are shown. Inclusion of ages 45–54 reveals that the reduction in the morbidity rates for males is not limited to

TABLE VI.—*Annual Age-specific Morbidity Rates Per Million for Each Sex*

Classification	Age Group	Males		Females	
		1935–9	1945–9	1935–9	1945–9
Tongue	45–	39	24	8	11
	55–	154	73	14	24
	65–	374	264	19	43
	75–	311	270	10	71
Main oral cavity	45–	37	18	10	11
	55–	145	64	27	27
	65–	369	206	25	41
	75–	345	297	30	34
Faucial region	45–	21	16	2	1
	55–	126	44	2	3
	65–	342	176	7	6
	75–	320	230	10	19

the older ages, but is demonstrable in varying degrees in each group. Within each anatomical site the greatest proportionate decrease for males is to be observed at ages 55–64. It is noticeable, too, that the age-specific rates in the second series assume an upward trend, whereas in the earlier period the peak occurred at ages 65–74.

Despite the comparatively low rates for females resulting from the breakdown of each anatomical group into ages, the fact emerges clearly that the increase in the incidence of cancer of the tongue is apparent at younger ages, although it is most striking at ages 75 and over, where it exceeds one-quarter of the rate experienced by males.

The increased rate for the faucial region is also seen to be concentrated in the highest age group. Actually, at the lower ages the trend is slightly in the opposite direction, but, as already mentioned, where the incidence is so low some fluctuation is to be expected and is comparatively unimportant. A moderate and slightly erratic change in rates is observed for the main oral cavity, the greatest difference being in the 65–74 age group.

The trends shown in Table VII make it clear that in general for both sexes the "risk rate" for the incidence of cancer of the mouth has undergone a striking change. The calculated risks for separate age groups from 45 years upwards are given. Although, of course, precision cannot be attained in any calculations based solely on hospital registrations, these figures can probably be accepted as reliable trends.

TABLE VII.—*Changes in Cancer "Risk Rate" (Expressed as Ratio of 1 Case Arising in Number of Persons Specified in Each Age Group)*

Classification	Age Group	Males		Females	
		1935–9	1945–9	1935–9	1945–9
Tongue	45–	25,400	42,400	128,200	88,500
	55–	6,500	13,600	72,500	42,000
	65–	2,700	3,800	51,800	23,500
	75–	3,200	3,700	100,000	14,100
Main oral cavity	45–	26,700	54,600	99,000	95,200
	55–	6,900	15,600	37,600	36,500
	65–	2,700	4,900	40,700	24,200
	75–	2,900	3,400	33,200	29,400
Faucial region	45–	47,400	63,700	625,000	1,250,000
	55–	7,900	23,000	500,000	370,400
	65–	2,900	5,700	142,900	158,700
	75–	3,100	4,400	100,000	54,100

Differential Rates in Urban and Rural Areas

The final factor investigated is differential morbidity rates for the types of local authority areas in which patients resided. Analysis in these terms yields the annual rates given in Table VIII. Although sub-analyses relate to smaller

TABLE VIII.—*Standardized Annual Morbidity Rates Per Million at All Ages for Local Authority Areas*

Type of Local Authority	Males		Females	
	1935–9	1945–9	1935–9	1945–9
County boroughs	178	98	13	19
Municipal boroughs and urban districts	104	69	11	15
Rural districts	71	43	17	10
Total	138	79	12	17

population groups, the rates throughout have been shown on a "per million" basis to maintain consistency with earlier tables. They have been standardized for comparability, the age distribution of the population in the surveyed area in the mid-year of 1935–9 period having been used as the standard. In this process an arbitrary assumption has been made that the age constitution of the aggregate of each type of local authority area is the same as for England and Wales, excluding Greater London.

Table IX shows the changes in morbidity rates expressed as percentages. These figures indicate that for males the decrease has occurred in each kind of community, but is

TABLE IX.—*Changes in Standardized Morbidity Rates for Local Authority Areas Over a Decade*

Type of Local Authority	Percentage Difference	
	Males	Females
County boroughs	−50%	+46%
Municipal boroughs and urban districts	−34%	+36%
Rural districts	−39%	−41%
Total	−43%	+42%

particularly striking in the county boroughs, where it amounts to 50%. Conversely, for females an increase of 46% has occurred in the county boroughs. In the municipal boroughs and urban districts the increase of 36% for females is likewise of the same order as the corresponding decrease of 34% for males. Only in the rural districts does the female rate show a decrease, the figure being 41%, whilst the corresponding one for males is 39%. This decrease for females is attributable to the fact that in the earlier period the rate was, rather surprisingly, higher in the rural districts than in the other communities. It must be remembered, however, that the rural population in the surveyed area is comparatively small and rates are consequently more liable to chance fluctuation.

The long time-lag between the inception of cancer and its clinical manifestation necessitates caution in the precise deductions to be drawn from differential rates unless there is full knowledge of the exact period of time over which individual patients have been resident in a particular region. In the surveyed area the population aggregate in the county boroughs fell by nearly 4% during the decade : other urban populations rose by nearly 14%, and rural districts by just over 5%.

Despite such impediments, it seems logical to deduce from the analyses that : (*a*) residence in the most urbanized communities results in intensification of certain aetiological hazards for both sexes ; (*b*) an aetiological factor not solely related to the degree of urbanization has become less potent for men ; and (*c*) an aetiological factor not apparently operating in the rural districts has become more pronounced in the case of women.

Discussion

Inherent in the diverging morbidity trends for males and females in the area surveyed is an apparent paradox when the findings are considered in relation to the contrary trends for the sexes following treatment of cancer of the mouth (Russell, 1954). In men the incidence of the disease has decreased, although they have previously been shown to exhibit a worse response to treatment and to be more prone than women to develop metastases ; in women there is greater vulnerability so far as incidence is concerned, but a higher rate of recovery and of resistance to dissemination of the disease.

The age-specific trends for males, which yield a lowered incidence of varying degrees throughout the entire range from 45 years upward, suggest the removal or diminution of aetiological factors the influence of which is operating from early adult life. Two factors could conceivably be partly if not necessarily wholly responsible—namely, improvements in the control of syphilis and in the incidence of oral leucoplakia. Whether smoking habits have any relevance is perhaps more speculative, although it is of interest that in a mortality survey based on English and Welsh County Boroughs Buckatzsch and Doll (1952) reported an inverse relationship in 1921–30 between cancer of the tongue and lung.

It is conventional to regard the incubation period for cancer as 20 years. Reference has previously been made (Paterson, Tod, and Russell, 1950) to the hypothesis that, in men, local aggravation is a relevant factor in susceptibility to the disease, but that in women a systemic factor, such as microcytic anaemia, is responsible. If these criteria be accepted in postulating possible reasons for the higher incidence rate in women, it may well be profitable to investigate their proclivity for microcytic anaemia in, say, South-east Lancashire.

South-east Lancashire was predominantly a textile area until about the middle of the 1930–9 decade, when, as a result of severe and prolonged trade recession, other industries were gradually developed. Social conditions from about the middle of the 1920s cannot be ignored and may have some significance in this context.

It is tempting to attach some credence to this theory by studying unemployment rates, which, although showing some variation in degree and period in different sub-areas, in general compared very unfavourably with the average for the country. Whilst investigating morbidity trends in the individual sub-areas, it was noticed, for example, that—unlike most other towns—in the County Borough of Oldham the main changes in incidence did not emerge in the 1945–9 period but have done so in the 1950s.* In this district the highest unemployment rate of about 50% occurred in 1931 (Lancashire Industrial Development Association, 1950)—an interval which corresponds closely with the twenty-year incubation period.

*A separate survey of the National Health Service period is being prepared, it having been considered preferable, for purposes of comparison, to confine the present investigation to a period prior to the N.H.S. having become fully effective.

Unfortunately, morbidity trends for microcytic anaemia have not been obtainable on a statistically reliable basis and mortality trends are not helpful, as deaths would be certified to the sequelae and not to the predisposing condition. Despite the lack of statistical support, physicians of long experience in the textile area express the view that anaemia was more prevalent in women over twenty years ago than in many other communities.

The age-specific rates for women suggest that some influence has begun to affect them to a greater extent at the period of life which broadly coincides with the menopausal ages.

It is worth while to take cognizance also of the fact that in these textile communities about 90% of the water supply is predominantly "soft." Women are much more susceptible to the incidence of diseases of the thyroid gland than are men : recent investigations on endemic goitre and cancer (Murray, Ryle, Simpson, and Wilson, 1948 ; Stocks, 1947) have indicated a greater susceptibility to both conditions in areas with soft or, conversely, very hard water, with less susceptibility where the drinking-water is moderately hard.

It is interesting to observe that the extent of the divergence in sex-morbidity trends for cancer of the mouth, irrespective of variation within anatomical subgroups, is almost identical —that is, −43% for males and +42% for females. It seems clear that the degree of urbanization is a pertinent factor, and it becomes increasingly apparent that in cancer of the mouth, as in cancers of other sites (Registrar-General, 1954a), residents of both sexes in rural districts compare advantageously with those in other urban communities.

Analysis by occupation and social class has not, unfortunately, been practicable in retrospect owing to the lack of sufficiently precise and adequate information in the earlier years. Consequently, no attempt has been made to investigate other factors of interest, such as the possible relevance of certain practices performed in the textile industry, which have tended to become less frequent.

Morbidity surveys for cancer of the mouth, planned on comparable lines for various kinds of communities, would obviously be preferable to mortality statistics as a basis for the study of aetiological factors, valuable though the latter are for many purposes. There is some evidence that the lower incidence for males is not confined to this country, as, for example, in a French study of cancer of various sites (Denoix *et al.*, 1954), where reference is made to an apparent decrease in cancer of the tongue for males.

It seems reasonable to deduce that amelioration of the cancer problem is to be sought in the field of preventive medicine. On this assumption it seems logical to advocate that any genuine decrease in incidence merits equally assiduous attention as an observed increase.

Summary

Morbidity rates for cancer of the mouth in each sex, based on registrations of patients at the Christie Hospital and Holt Radium Institute, Manchester, and its peripheral clinics in the Manchester Regional Hospital Board area during the periods 1935–9 and 1945–9, are calculated.

The standardized trends over a decade show a marked decrease in the incidence of cancer of the mouth in men, and an increase in the disease in women. The extent of these diverging trends is almost identical.

Differential analyses of morbidity rates are conducted on an age-specific and local authority area basis.

Possible aetiological factors are discussed, and the desirability of intensifying research along preventive lines is advocated.

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REFERENCES

Buckatzsch, J., and Doll, R. (1952). *J. Hyg. (Lond.)*, **50**, 384.
Denoix, P. F., *et al.* (1954). *Monographie de l'Institut National d'Hygiène*, No. 5.
Lancashire Industrial Development Association (1950). Industrial Report No. 5: The Spinning Area.
Mackay, D. (1951) *Studies on Medical and Population Subjects*, No. 4. H.M.S.O. London.
Minister of Health (1954). Annual Report for the year 1953, Part II.
Murray, M. M., Ryle, J. A., Simpson, B. W., and Wilson, D. C. (1948). *Med. Res. Coun. Mem.*, No. 18. H.M.S.O., London.
Paterson, R., Tod, M. C., and Russell, M. H. (1946). *The Results of Radium and X-ray Therapy in Malignant Disease* (Second Statistical Report). Livingstone, Edinburgh.
—— —— —— (1950). Ibid. (Third Statistical Report). Livingstone, Edinburgh.
Registrar-General of England and Wales (1938). *Statistical Review for the Year 1937*; Tables, Part I. Medical. H.M.S.O., London.
—— (1947). *Statistical Review for the years 1938 and 1939*; Text. H.M.S.O., London.
—— (1949). *Statistical Review for the Year 1947*; Tables, Part I. Medical. H.M.S.O., London.
—— (1953). *Statistical Review for the Years 1948 and 1949*; Text, Medical. H.M.S.O., London.
—— (1954a). *Statistical Review for the Year 1951*; Text Volume. H.M.S.O., London.
Russell, M. H. (1954). *British Medical Journal*, **1**, 430.
Stocks, P. (1947). *Studies on Medical and Population Subjects*, No. 1. H.M.S.O., London.

TREATMENT OF PEPTIC ULCERS WITH "ROTER" TABLETS

BY

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"Roter" tablets were introduced into this country from Holland in 1948 for the treatment of peptic ulceration, and are still widely prescribed in spite of being classified in Group 6 by the Cohen Committee. Tablets with similar formulae are being manufactured in this country under the names tabs. bismuth subnitrate co. (B.D.H.; Kirby), tabs. stomachic co. (Duncan, Flockhart), and tabs. frangula co. (Evans; Woolley; Cuxson, Gerrard). No report on their use has appeared in the British medical press, but in view of the fact that the tablets contain bismuth subnitrate, which has the reputation of causing serious toxic effects, the need for an inquiry into their use is indicated.

Composition.—The tablets contain magnesium carbonate pond. (400 mg.); sodium bicarbonate (200 mg.); calamus (25 mg.), an aromatic bitter said to act as a carminative (*B.P.C.* 1923); frangula, which has a mild purgative action similar to cascara (*B.P.C.* 1954); and bismuth subnitrate (350 mg.), which is widely prescribed on the Continent for dyspepsia, although its action is unknown. In recent years bismuth subnitrate has fallen into disrepute in this country and America following the publication of reports of a number of fatal cases of nitrate poisoning. Marcus and Joffe (1949) stated that the use of bismuth subnitrate as a therapeutic agent is unnecessary, unwarranted, and hazardous.

Material

The clinical material for these notes was derived from my general practice in Hawick, Scotland (population 17,000), famous for its hosiery industry, which employs a large number of both married and single women. The number of patients at risk in this series is 3,700, and the period of observation is one year. The cases treated include 79 which presented with active symptoms of peptic ulcer, proved radiologically, and 19 of "presumptive peptic ulcer" (Doll and Avery Jones, 1951), with a history suggestive of peptic ulcer, in which the barium-meal examination was negative.

Incidence of Peptic Ulcer

The overall incidence of active ulcer (Table I) in this series is 2%, or 2.9% over the age of 20, which is in general agreement with Ivy *et al.* (1950), who quote a figure of 1–3% for the latter age group. Table I further illustrates that the condition is more common between the ages of 35 and 54, and after 55 the incidence is reduced by one-half in both men and women.

TABLE I

Ages:	0–14	15–19	20–34	35–54	55+	Totals
Total population	774	188	760	1,016	963	3,701
Active ulcers ..	0	0	19	42	18	79
% with ,, ..	0	0	2·5	4·1	1·9	2·0
Presumptive ulcers	0	0	6	9	4	19
Total ,,	0	0	25	51	22	98
% with ,,	0	0	3·3	5·0	2·3	2·6
Male	395	80	354	446	354	1,629
Active ulcers ..	0	0	13	31	12	56
% with ,, ..	0	0	3·7	6·9	3·4	3·4
Female	379	108	406	570	609	2,072
Active ulcers ..	0	0	6	11	6	23
% with ,, ..	0	0	1·5	1·9	1·0	1·1

The sex ratio of active ulcers is 3 male to 1 female, and of five new cases presented during the year four were women. An unusual feature is the low incidence of gastric ulcers, only two cases occurring in the whole series.

The average duration of symptoms in the active ulcer group, dating from the first attack of indigestion, was 12 years: 25 patients (18 M., 7 F.) with a history of less than 5 years, 38 patients (27 M., 11 F.) with a history of less than 10 years, and 41 patients (29 M., 12 F.) with a history of over 20 years.

Previous treatment comprised advice regarding diet and frequent feeds, with the addition of magnesium trisilicate powder and small doses of phenobarbitone. The main cause of unsatisfactory results was failure on the part of the patient to adhere to the dietary restrictions.

Method and Dosage

The tablets used were specially prepared by F.A.I.R. Laboratories, varying in shape from the original tablets and bearing no trade name. The patients were instructed to take two tablets three times a day after food for three weeks; thereafter one tablet three times a day for a period of two months. Fifteen cases with a long history of frequent relapses were instructed to continue on a maintenance dose of two tablets daily for the full period of one year. This is below the dosage recommended by the makers, who suggest two tablets three times a day for the first three months, followed by one tablet three times a day for the next three months, and thereafter one tablet daily for a further three months.

All but five of the 98 cases were ambulant throughout their treatment and no instructions were given as to rest. They were advised to take an average diet but to avoid fried foods.

Results

The immediate clinical results were assessed after the first month's treatment in four main groups: (A) pronounced relief (symptom-free); (B) definite relief (minor symptoms with no pain); (C) doubtful relief (symptoms persisting but improved); (D) no relief.

Table II shows that 81% of cases became symptom-free—70% of them during the first week and 30% during the second week; a further 9% were relieved of the majority of their symptoms. Thus there was a satisfactory response in 90% of cases.

Four of the nine cases in groups C and D have elected to go to surgery, and one of the remaining cases has a hiatus hernia as well as a duodenal ulcer. Experience of treating these "failures" over the past six years leads one to believe that no form of medical treatment will be effective and that surgery is the only hope of relieving their symptoms. In 75% of the cases the patients were of the opinion that the

Table II

Group	Active Ulcers	Presumptive Ulcers	Totals
A	63 (79·6%)	17 (89·0%)	80 (81·7%)
B	8 (10·2%)	1 (5·5%)	9 (9·2%)
C	6 (7·6%)	1 (5·5%)	7 (7·1%)
D	2 (2·5%)	0 (—)	2 (2·0%)
Totals	79 (100%)	19 (100%)	98 (100%)

tablets were superior to alkaline powders, and they found that they were able to take foods which they had avoided for years.

The absence of controls is unfortunate, but their use in general practice is beset with difficulties, and recently the Medical Defence Union has advised the College of General Practitioners that patients should be advised when controls are being used. However, Ivy *et al.* (1949) have pointed out that in a chronic condition such as peptic ulcer it is possible to use the patient as his own control, working on the assumption that a patient who shows a pattern of frequent recurrence over a period of four years or longer is unlikely to show spontaneously a marked diminution of frequency of recurrence on ambulant management.

Fifteen cases with an average duration of symptoms of 10 years have been kept on a maintenance dose of two roter tablets a day for one year, and a record kept of the number of relapses—a return of even mild ulcer distress constituting a relapse. This was compared with the number of relapses recorded in the previous year. Patients shown with "six" relapses a year were known regular attenders at the surgery, and, although stating that their discomfort was more or less continuous, averaged six acute episodes. Table III shows that with this regime there was a reduction in the number of relapses from an average of four a year to less than one a year. Those which did occur rapidly responded to increased dosage.

Table III

Age	Duration of Symptoms (Years)	Relapses	
		1953	1954
39	10	(6)*	1
51	11	(6)	Nil
43	8	(6)	1
41	16	(6)	1
38	4	5	1
35	10	5	1
52	12	5	Nil
29	10	4	1
42	4	4	2
44	18	3	Nil
43	18	2	"
25	5	2	1
37	7	2	1
31	9	2	Nil
37	8	2	1
Averages: 40	10	4	0·73

* Average of acute episodes.

The relapse rate at the end of one year in a further 43 cases (group A) whose treatment was stopped at the end of three months was 57%; however, as patients were instructed to report immediately on return of symptoms, many of these were mild and in each case responded satisfactorily to further treatment.

Toxic and Side-effects

Possible toxic effects from the use of roter tablets arise from their content of bismuth subnitrate, although the intake of 0.7 g. is within the limits set by the *B.P.C.*

The literature contains numerous references to methaemoglobinaemia following its use: Miller (1945), in a review of the subject, quotes six cases, four of which were fatal. Since then further cases have been reported by Wallace (1947) and Marcus and Joffe (1949). Analysis of these cases shows that all but one of the fatalities occurred in infants aged 1 week, 3 weeks, 5 weeks, 1 month, and 1½ years. The adult suffered from intestinal obstruction. Diarrhoea was present in five of the cases, and in three the bismuth subnitrate was administered rectally. Thus it appears that, while bismuth subnitrate may be highly toxic in infants, particularly in the presence of diarrhoea, its use in adults is not contraindicated, and the statement of Marcus and Joffe, quoted by Martindale (1952), is unduly pessimistic.

Methaemoglobinaemia arises from the conversion of the nitrates into nitrite by nitrate-splitting organisms in the intestine. The urine and faeces were tested daily after the taking of two roter tablets three times a day for two months, but no nitrites were detecting using the α-naphthylamine sulphanilic acid method. This, however, may be due to the destruction of the nitrites by other micro-organisms, as pointed out by ZøBell (1932). Two patients, however, complained of a "thumping headache," which ceased when the drugs were withheld, raising the possibility of nitrite being actively present in the blood stream. The stools became "muddy"-coloured owing to the presence of bismuth, but this can be easily distinguished from the "tarry" black stool of a melaena; benzidine tests of the stools were negative, although a very late positive does sometimes occur. Three patients complained of diarrhoea, due possibly to frangula, requiring the tablets to be withheld in one case. Thus, in the 98 cases treated, no serious toxic effects have been observed, and the roter tablets appear to be safe in the doses recommended.

Comments

Psychologically, roter tablets are an ideal drug, combining the essentials of expensiveness, taste, and colour with an unusual discoloration of the stools following their use; and we are presented with the problem of how much their effect is purely psychological and how much due to physical properties as yet unknown. Little information is obtained from a study of the individual drugs. The content of magnesium carbonate and sodium bicarbonate is too small to have any effect on the gastric juice, while calamus appears to be contraindicated in view of its action as a bitter, and the only known effect of frangula is to relieve constipation. The effect of bismuth subnitrate demands more attention. Used in the treatment of dyspepsia since its introduction by Odier in 1776, it is still widely prescribed on the Continent, where it is preferred to the carbonate. It has been suggested that, like the carbonate, it lines the ulcer; yet Pygott (1954), using 20 g. of bismuth carbonate, was able to demonstrate this in only two out of nine cases of duodenal ulcer. The effect on the stomach of the slow but continuous absorption of nitrite has not yet been investigated, although Brun (1942) reports the relief of ulcer pain following the use of glyceryl trinitrate, and Steiglitz (1928) has used this effect of bismuth subnitrate in the treatment of hypertension. The therapeutic tests are handicapped by the absence of controls, but a 90% satisfactory response obtained in ambulant patients in the absence of dietary restriction or other drugs is encouraging; and the reduction of the average number of relapses in the 15 patients kept on a maintenance dose confirms my own view that the beneficial effect of roter tablets cannot be explained on purely psychological grounds. A 57% relapse rate at the end of one year in those cases receiving only three months' treatment indicates that roter tablets do not influence the relapse rate in the dosage given, although in part this may be due to inadequate dosage.

The treatment is ideal for general practice, where its simplicity appeals to both patient and doctor, and, although its mode of action remains an unsolved problem, this should not deter its use in a condition the cause of which remains a riddle. Finally, while the possibility of toxic effects does arise, none have been reported or found in this series; but, as a precaution, the tablets should not be administered to young children.

Summary

Seventy-nine cases of peptic ulcer and 19 of presumptive peptic ulcer have been treated with roter tablets. Immediate clinical response was satisfactory in

90% of patients, with a relapse rate of 57% in the first year; a reduction in the average number of relapses was recorded in 15 cases kept on a maintenance dose for one year. The mode of action of the tablets and the possibility of toxic symptoms arising are discussed.

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References

Brun, G. C. (1942). *Acta med. scand.*, **110**, 416.
Doll, R., and Jones, F. Avery (1951). *Spec. Rep. Ser. med. Res. Coun. Lond.*, No. 276, p. 24.
Ivy, A. C., *et al.* (1949). *Gastroenterology*, **12**, 735.
—— Grossman, M. I., and Bachrach, W. H. (1950). *Peptic Ulcer*, p. 608. London.
Marcus, H., and Joffe, J. R. (1949). *New Engl. J. Med.*, **240**, 599.
Martindale (1952). *The Extra Pharmacopoeia*, **1**, 286. London.
Miller, G. E. (1945). *Gastroenterology*, **4**, 430.
Pygott, F. (1954). *Lancet*, **1**, 1314.
Steiglitz, E. J. (1928). *J. Pharmacol.*, **32**, 23.
Wallace, W. M. (1947). *J. Amer. med. Ass.*, **133**, 1280.
ZøBell, C. E. (1932). *J. Bact.*, **24**, 237.

THE TREATMENT OF SIMPLE RIB FRACTURES

A CRITICISM OF A "LAISSEZ-FAIRE" POLICY

BY

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The treatment of simple rib fractures appears to have remained unchanged for many years, and has commanded no great attention among recent surgical writings in this country. Strapping, binding the chest, or some other form of support remains the sheet anchor in therapy as recommended by the majority of writers. This article draws attention to the frequency with which these fractures occur, and advocates a better method of initial treatment; it is concerned only with simple uncomplicated rib fractures, and not with crush injuries of the chest.

About 80 cases of simple rib fractures are seen every year in this unit, and it is calculated that about 15,000 occur every year in Great Britain. This represents a formidable mass of suffering and disability, sufficient to justify far more care and attention than this problem usually receives.

Most medical students in this country seem to be taught to use some form of strapping as the main and usually the only method of treatment, while 33 out of 40 British and American surgical textbooks which have been consulted make similar recommendations.

A Criticism of Strapping

As a method of treatment for these fractures I believe strapping of any type has several major disadvantages.

1. *It is an Inefficient and Inadequate Method.*—I do not believe it is ever possible to immobilize a rib fracture completely except by internal fixation, which indeed is advocated by certain American writers for this very reason. Strapping provides inadequate support, only partial immobilization, and fails to stop the acute pain suffered with every full inspiration, attack of coughing, or energetic movement. One of the pressing worries to the patient is inability to sleep with any degree of comfort, a complaint of which hardly any mention is ever made in standard textbooks. I have seen patients bound in strapping who still cannot sleep at all adequately or comfortably two or three weeks after the injury. A method of treatment which fails to ensure a good night's rest two or three weeks after the injury should be discarded.

2. *It is an Uncomfortable Method.*—Nearly every patient from whom I have removed previously applied strapping has been profoundly relieved to be rid of it. Many find it extremely irritating, and a high proportion develop skin rashes under the strapping, even in a few days. This point, too, is glossed over in most textbooks.

3. *It is a Lazy Method.*—Undoubtedly many doctors apply the strapping themselves; quite certainly, many delegate it usually to one of the nursing staff. To give an order is in this case less trouble than to carry it out.

4. *It may even be a Dangerous Method.*—Hirsh and Ellis (1940) record the cases of two patients who developed bilateral oedema of the legs and ankles following fixation of the chest for rib fractures. While this must be a rare occurrence, it is yet a warning of what can happen.

Injection as a Primary Treatment

Zoppi (1936) was apparently the first to advocate local analgesic injection, using procaine. Strong support for this came from Hamon *et al.* (1942), and Smith (1942) drew attention to two distinct causes of pain: (1) the dull ache of muscle and ligamentous injury, and (2) the sharp stabs of bone pain. Other writers in favour are Homans (1945), Bancroft and Murray (1945), Ferguson (1947), Naylor (1952), and Belsey (1953). Roualle (1952) suggested using "efocaine" as a long-acting analgesic, while Winkler (1951) used a long-acting analgesic in treatment by means of intercostal nerve blocks. Yet, despite this not inconsiderable body of evidence in favour of injection treatment as a primary procedure, what Belsey calls the "time-honoured treatment by strapping" remains the predominantly taught and, I believe, practised treatment in this country. In my opinion it is a method honoured by nothing but time.

Smith's paper first brought injection treatment to my notice some years after its publication; he pointed out that, although in theory one injection of a short-acting analgesic such as procaine should last for only a few hours, in practice it often sufficed to relieve bone pain not only completely but permanently. For a number of years I treated these fractures by direct injection into the fracture site of 1–2 ml. of 2% procaine with no external support whatever, and was satisfied that Smith's claims were fully justified. More recently a long-acting local analgesic was substituted, using a benzocaine-urethane solution as advocated by Rutter (1952).

During the early months of this year efocaine was used for direct injection to each fracture site, but although no untoward sequelae have occurred the use of efocaine has now been abandoned in favour of the benzocaine-urethane solution in view of the serious complications reported by Clarke *et al.* (1955) and Parsonage *et al.* (1955).

I believe injection is the treatment of choice in almost every patient; it abolishes bone pain completely and it can be easily repeated if necessary. Injection takes no longer than does the application of strapping, there is no interference with the patients' bathing, and they can sleep in comfort.

The symptoms and signs of these fractures are adequately described in textbooks and need not be reiterated here, but the most important and valuable finding does not normally receive adequate emphasis. This is extreme local tenderness at the fracture site. Smith stressed this years ago, and I am convinced it is of fundamental importance. The patient who is thoroughly bruised but without a fracture does not have this extreme *local* tenderness; in those with a fracture one can accurately locate the fracture site(s) in a few moments.

Use of Radiographs in Rib Fractures

It is commonly advised that every suspected rib fracture should be radiographed, and it is often admitted that only 50% of these fractures are seen on the *x*-ray plates. I believe the true figure is much smaller and that too much importance is placed on *x*-ray films in uncomplicated rib fractures, despite their supposed importance from the

medico-legal viewpoint. At least 50% of cases which give adequate clinical evidence of fracture(s) are liable to be classified as "no fracture seen." The *x*-ray pictures are virtually of no help in defining *accurately* the site(s) of fracture for injection purposes. The basic principle that patients should be treated on clinical grounds and not on *x*-ray findings is just as true with rib fractures as elsewhere in medicine and surgery. A patient with a history of injury to the chest; acute pain made worse by coughing, deep breathing, and forced movements; a positive compression test; and, of most importance, acute local tenderness over one or more ribs should be treated as having rib fractures whether or not the *x*-ray films show any positive evidence of this. Were it not for the medico-legal aspects, and perhaps even despite these, I believe that most chest *x*-ray examinations for suspected rib fractures are a waste of time and money as well as uncomfortably delaying the one treatment which can really relieve the patient's pain. If there is any suspected complication, such as a concomitant lung injury, then, of course, *x*-ray examination is imperative.

Technique of Injection Treatment

The patient is stripped to the waist and lies on the unaffected side on a couch with the arm of the affected side stretched above the head; this arm position makes identification of the fracture site(s) considerably easier. When the patient has pointed to the painful area, this is examined by most careful palpation and one or more points of extreme local tenderness are found. A skin mark at each site is then made; here a ball-point pen is useful. If the fracture is lateral the patient remains in the lateral position, if more posterior he is placed in a more prone position, and if more anterior a more supine position is adopted. After cleansing the skin a subcutaneous weal is raised with 1% procaine and through this another needle is inserted directly down to the bone, which is quite easily felt. Then 2 ml. of benzocaine-urethane solution is injected at this level, and the skin puncture is covered by a touch of collodion. Each fracture is treated by a separate injection. No supportive strapping or bandages are subsequently applied.

Illustrative Cases

Several patients treated in the past three months have not been seen until two, three, or even four weeks after the injury, having previously been treated by strapping. Most of them, however, have been given the benefit of local injection, even at this late stage, and none have failed to show considerable symptomatic improvement. But, in order to be most effective, the injection should be given as soon as possible after injury; at a later stage organization of the haematoma at the fracture site may limit the penetrating power of the local analgesic.

A man of 71 was admitted after a road accident in which he sustained fractures of the right clavicle, right seventh and eighth ribs, right fifth metacarpal, and right tibia (double, comminuted). When first seen his main complaint was of acute pain in the right side of the chest. His rib fractures were injected within five hours of the injury, with immediate benefit. An hour later he complained for the first time of pain in the right leg, which at that time was still in a temporary box splint. His rib pain was so dominant that until it was abolished he was not conscious of acute pain from his tibial fractures.

A woman of 54, seen twenty days after fracturing her eighth left rib, had been routinely strapped. She still had pain on coughing and still slept badly. Injection entirely relieved her pain; she did not trouble to keep her next appointment, and was not seen again until asked to attend two months later; one injection had relieved her cough pain and enabled her to sleep properly again, even though it was not given until nearly three weeks after the injury.

A man of 60 fractured his right fifth to eighth ribs and was seen on the eighth day. His strapping was removed and each fracture site was injected. At that time coughing and deep breathing were painful and he was off work. He failed to return until sent for, when he admitted that his relief from injection had been immediate and permanent, and that within five days of injection he had been at work lifting 88-lb. (40-kg.) cheeses.

A woman of 40, six months pregnant, was seen fourteen days after a severe bout of coughing had produced acute pain in the left side of the chest. She was forced to sleep propped up on several pillows, and had obviously sustained a cough fracture. Injection relieved her pain and she was able again to sleep in a normal position. Birch (1954) recommends strapping for cough fractures in pregnancy. Injection gives a far better result.

A woman of 79 had had a series of operations on her right hip-joint, following a femoral neck fracture. While at home a severe fit of coughing produced acute pain in the right side of the chest. She was treated for strained muscles. Three weeks later, attending with regard to her hip-joint arthroplasty, she had pain on coughing, deep breathing, and forced movements, and was diagnosed as suffering from cough fracture of the right tenth rib. Injection produced immediate pain relief.

Injection Treatment and the General Practitioner

A frequent sequence of events following rib injury is for the patients to consult their own doctor and be referred then to hospital for *x*-ray examination for ? rib fracture. Two, three, or four *x*-ray pictures are taken and strapping is applied, usually in the casualty department. If the patients are elderly they may require admission. Those of working age are often off work for a month or more. Meanwhile the dismal sequence of painful days, sleepless nights, and a chest wall irritating under constricting strapping is their lot. Complaints of overcrowded out-patient departments and of hospitals undertaking an undue proportion of the treatment of many conditions are frequently encountered. Here is one condition in which the hospitals could hand back the patient's treatment to the general practitioner. Why should he (or she) not undertake primary injection of the rib fracture with a long-acting analgesic, and then, and only then, refer the patient for *x*-ray examination if such be considered necessary on medico-legal grounds? This would save the patient much unnecessary pain and delay and facilitate a much earlier return to work or household duties, the *x*-ray department would be spared in many cases, and for some patients it would avoid the necessity of hospital admission.

Medical students should be taught injection treatment as a routine procedure. Any concern regarding dangers due to lack of practice could be avoided by trial runs in the dissecting or post-mortem rooms.

Summary and Conclusions

Many thousands of patients sustain simple rib fractures every year in this country. Most of them appear to be treated by some form of strapping, which does not abolish their bone pain; they lose weeks of working time and often cannot sleep properly for long after the injury. Strapping as a method of treatment is outmoded and should be abolished in almost every case and replaced by the injection at each fracture site of a long-acting analgesic. Many of these injections could be given by the patient's own doctor, thus avoiding visits to hospital. *X*-ray films are of doubtful value and serve little purpose in most cases of simple rib fractures.

I thank Mr. R. C. F. Catterall and Mr. R. H. V. Hafner for permission to treat patients under their care, and for their help and advice.

REFERENCES

Bancroft, F. W., and Murray, C. R. (1945). *Surgical Treatment of the Motor Skeletal System*. Lippincott, Philadelphia.
Belsey, R. (1953). *Practitioner*, **170**, 138.
Birch, C. A. (1954). *Emergencies in Medical Practice*, 4th ed. Livingstone, Edinburgh.
Clarke, E., Morrison, R., and Roberts, H. (1955). *Lancet*, **1**, 896.
Ferguson, L. K. (1947). *Surgery of the Ambulatory Patient*. Lippincott, Philadelphia.
Hamon, P. H., Baker, D. R., and Kornegay, R. D. (1942). *J. Amer. med. Ass.*, **118**, 30.
Hirsh, B., and Ellis, R. (1940). *British Medical Journal*, **2**, 593.
Homans, J. (1945). *Textbook of Surgery*. Thomas, Springfield, Illinois.
Naylor, A. (1952). *Fractures and Orthopaedic Surgery for Physiotherapists and Nurses*, 3rd ed. Livinstone, Edinburgh.
Parsonage, M. J., Taverner, D., and Wooler, G. H. (1955). *British Medical Journal*, **1**, 1322.
Roualle, H. L. M. (1952). Ibid., **2**, 1293.
Rutter, A. G. (1952). Ibid., **2**, 1418.
Smith, D. J. N. (1942). Ibid., **1**, 383.
Winkler, V. L. (1951). *Wien. med. Wschr.*, **101**, 692.
Zoppi, B. (1936). *G. veneto Sci. med.* **10**, 666.

THE PAINFUL HEEL

BY

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In orthopaedic surgery there are several conditions which, though not serious diseases, are not welcomed by the orthopaedic surgeon on account of their intractable nature. Though confident instructions are often given for the treatment of these conditions in textbooks, in practice the results of orthodox treatment are frequently disappointing both to the surgeon and to the patient, and it is therefore a matter of some relief when a method of treatment which appears to give consistently good results is discovered.

In my experience painful heel, of the type where the pain is located in the region of the postero-medial attachment of the plantar fascia to the os calcis, comes into this category, and, despite the use of various types of heel "sorbo" pads to take the weight off this area, the elevation of the heel of the shoe, or even erasion of the tender area surgically, the results are usually disappointing. The fact that a surgical attack upon a calcaneal spur had proved successful was considered important enough for a case to be shown at a London orthopaedic club (*J. Bone Jt Surg.*, 1954).

It is almost universally agreed, however, that the condition is one of chronic strain of the posterior end of the central part of the plantar fascia, initiated or aggravated by toxic conditions on some occasions, and sometimes associated with the presence of a calcaneal spur on the *x*-ray film. It is also now widely appreciated that the presence of such a spur is probably only the sign of there being, or having been, a chronic strain in this area, and that such spurs frequently exist without any symptoms either past or present. In the days when this spur was regarded as the cause of the pain, the logical method of treatment was to remove the pressure of the patient's body weight from this spiky area. Methods of treating the condition by heel pads are relics of that approach to the condition, but once it is appreciated that in fact the strain which causes pain in this area is a longitudinal one working in the line of the plantar fascia, then obviously some other method of minimizing this strain is required.

FIG. 1.—Plantar fascia after Gray. The insertion of the central part posteriorly on the medial side of the os calcis is to be noted. A, medial part; B, central part; C, lateral part.

Consideration of the anatomy of the plantar fascia (Fig. 1) shows that the main and apparently offending portion of the fascia is attached just medial to the vertical axis of the peritalar joint (Shephard, 1951). It seems logical, therefore, that the strain can be relieved by some form of insole which tilts the heel and relaxes this portion of the fascia.

For the past two years I have been using an insole (Fig. 2) originally designed, I believe, by Mr. A. O. Parker, of Cardiff, and designated by him a convex wedge. Whilst at first sight it would appear that this appliance presses on the plantar fascia and would increase the tension in the tender area, in practice the result of this treatment has been so consistently good that I would sooner abandon the theory of its effectiveness than the method of treatment.

In the past two years I have seen 17 cases of painful heel varying in duration from two to twenty-four months. All of these have been relieved by the use of this insole, and in all but three cases relief has been such that by the time the insole has worn out they have not required a further insole. It has therefore become my practice to supply this insole, see the patients again in six weeks' time for confirmation of the results of therapy, to ask them to wear the

FIG. 2.—View of the insole from the medial aspect.

insole until it wears out, and only to see me again if they are not cured in this time. All the patients have been willing to do this, as within seven days of having the insole they have found that relief is being obtained, and they feel confident that the condition is slowly but steadily being alleviated. In three cases where more than one insole has been supplied (in fact, up to date they have applied for only one replacement each) it has been to people who had the condition for a considerable time before receiving treatment and who are heavy walkers.

This insole was supplied to me by Messrs. R. Taylor and Son, 50, Bath Road, Walsall.

REFERENCES

J. Bone Jt Surg., 1954, 36B, 670.
Shephard, E. (1951). *J. Bone Jt Surg.*, 33B, 258.

PHARMACOLOGICAL STUDIES ON LEAD E.D.T.A.

BY

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AND

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A recent communication by Sapeika (1955) on use of "the water-soluble chelated compound lead ethylenediamine tetra-acetic acid" (Pb E.D.T.A.) as a contrast medium describes the intravenous administration of the disodium complex ($PbNa_2$ E.D.T.A.) to four human subjects. We wish here to record some animal experiments carried out at these laboratories in 1953, when we were investigating the potentialities of this substance for radiography, as well as some subsequent studies. Polarographic analyses showed that the samples of $PbNa_2$ E.D.T.A. used in our experiments contained less than 0.01% of ionized lead.

In aqueous solution, this chelated compound is decomposed by sulphides and forms a black precipitate; we were not surprised to find that the faeces of animals dosed with $PbNa_2$ E.D.T.A. turned black, as Sapeika recorded of his patients' stools, but we are not clear why he found it necessary to invoke enzymatic decomposition to account for the observation.

Toxicology and Excretion Rates

The acute intravenous LD_{50} of $PbNa_2$ E.D.T.A. was determined in two different strains of mice (A2G and GFF)

and gave values of 3.5 to 4.5 g./kg. The corresponding figure for diodone, still widely used as a contrast medium, was approximately 6 g./kg.

Excretion studies were carried out on adult female albino rats (WAG strain) and on rabbits. Six groups of three rats were given single doses of $PbNa_2$ E.D.T.A. by the oral, subcutaneous, or intraperitoneal route, two dose levels (100 and 500 mg./kg.) being used for each route. The faeces and urine from each group were collected separately each day for four days and then analysed for total lead polarographically.

On the first day after oral doses of 100 and 500 mg./kg., 2% and 3% respectively of the administered lead appeared in the urine, and thereafter this was free from lead. At the dose of 100 mg./kg. the remaining lead was excreted in the faeces during the first two days, but at the dose of 500 mg./kg. the total faecal recovery was only 88% over four days. After subcutaneous administration of 100 and 500 mg./kg. the urinary recoveries over four days were 79% and 82% respectively, the faecal recoveries being 6% and 12%. Although most of the urinary lead was recovered in the first day's voidings, there was still some present four days after the 500 mg./kg. dose. The four-day urinary recoveries after intraperitoneal injections at 100 and 500 mg./kg. were 70% and 50% respectively, the faecal values being 5% and 25%.

Fourteen days after treatment all the rats were killed; the organs of one rat from each group were examined histologically. There was evidence of slight renal damage (cloudy swelling of mid-zone and juxtamedullary tubules) with 500 mg./kg. This group had shown the highest urinary recovery and was still voiding lead on the fourth day. Apart from this finding, nothing abnormal was observed in any of the other rats. The liver, kidneys, gastro-intestinal tract, spleen, femur, and blood from a second rat in each group were assayed for lead. None was detected in these tissues in any of the rats killed fourteen days after dosing. All rats lost weight during the experimental period.

A further group of three young female rats were given single intravenous injections (100 mg./kg.) of $PbNa_2$ E.D.T.A. The excreta were collected for three days, when the animals were killed and their carcasses assayed for lead. The urinary and faecal recoveries were 85% and 8% respectively, 7% being found in the cadavers. The animals were still excreting small amounts of lead by both routes on the third day.

The excretion studies in rabbits were conducted as follows. Two adult rabbits in each of three groups were given single intravenous injections of $PbNa_2$ E.D.T.A. at levels of 100, 500, and 1,000 mg./kg. One rabbit on the highest dose died 24 hours later and the second after seven days. The remaining animals were killed one week after being injected. Except from the first rabbit, which of the total dose voided 71% and excreted 2% in the faeces before dying, the urinary and faecal excretions were measured for two days after administration. In this period the rabbit that died after seven days voided 87% and excreted 3%. The average urinary and faecal recoveries were 80% and 4% and 73% and 5%, for the animals dosed at 500 and 100 mg./kg. respectively. Histological examinations were made on the two rabbits that died and on one rabbit from each of the two other groups. There was evidence of hepatic and renal damage in the rabbits that died. The lungs and livers, and especially the kidneys, of the remaining two rabbits had clearly been affected by the drug, the degree of damage being related to dosage. Two further rabbits were given intravenous doses at 1,000 mg./kg. The first developed severe convulsions and screaming fits, and died two days later. After three days the second rabbit developed paralysis of the hind legs and was destroyed.

The urine from rabbits injected intravenously with $PbNa_2$ E.D.T.A. at levels of 100 mg./kg. or more gave positive reactions with benzidine. At 100 mg./kg. a positive reaction was obtained with the third day's voidings only, but at higher levels the test became positive within 16 hours of administration. There was no evidence of haematuria in rats given 1,000 and mice given 2,000 mg./kg. intravenously. It is interesting that Sapeika reports intravascular haemolysis in his fourth patient.

At this point it may be pertinent to mention the results of an *in vitro* experiment carried out by Mr. C. R. B. Joyce (private communication) at the London Hospital. $PbNa_2$ E.D.T.A. and $PbCl_2$ were compared for their effects on the mobility of K^+ ions in human erythrocytes suspended in physiological saline. The results showed that $PbNa_2$ E.D.T.A. was considerably less active than $PbCl_2$ in this respect, but that its effect was appreciable and increased with time.

Summary

Our results may be summarized thus. $PbNa_2$ E.D.T.A. did not appear to be unduly toxic to mice and rats and did not cause haematuria in them. Although most of the lead was eliminated via the kidney after intravenous administration, a small percentage appeared in the gut. Also, some of the drug appeared in the urine after oral dosing. Although lead could not be detected in the liver, kidney, alimentary tract, spleen, femur, or blood of rats dosed fourteen days earlier, it is obvious from the excretion rates that the time required for complete elimination from the body is considerably longer than it is for diodone. The effects of $PbNa_2$ E.D.T.A. on rabbits were disturbing. Doses of 1,000 mg./kg. were fatal, and at lower doses the drug produced haematuria and caused severe hepatic and renal damage.

The results of our earlier experiments, here recorded, led us to conclude that we should not be justified in submitting the substance studied to clinical trial, and the confirmation of its toxicity provided by the later investigations caused us to lose interest in it as a possible contrast medium.

Reference

Sapeika, N. (1955). *British Medical Journal*, 2, 167.

Medical Memoranda

Tuberculosis of Pubis Presenting as a Cold Abscess of the Thigh

The pubic bone is an uncommon site of tuberculous osteitis: it is not mentioned by Girdlestone and Somerville (1952). Small series of cases have been described in recent literature (Clavel, 1951, three cases; Mallo, 1947, one case; Ficai, 1949, two cases). Cold abscess formation from tuberculous osteitis of the pubis seems peculiarly rare. The following case presented as a cold abscess tracking down the thigh from the pubis.

Case Report

A married woman aged 23 was admitted to hospital in August, 1953, complaining of a lump in the inner aspect of the upper part of the right thigh which had slowly increased in size over the previous two months. It was painless, and had not interfered with movement. Her general health had been good and there was no loss of weight or cough. She had one child, aged 2, and no abnormal obstetric history.

Examination showed a fusiform tumour in the adductor region of the right thigh deep to the superficial adductor muscles. Its long axis measured 6 in. (15 cm.), and its upper pole was attached to the pubis. It had a uniformly firm consistency, the surface was smooth, and the edge was ill defined. It was not tender nor did it fluctuate or pulsate. The pubic bone was not tender. The patient's general condition was excellent.

Investigations.—*X*-ray examination showed clear lung fields and an area of bone resorption in the body of the right pubic bone; adjacent bones were normal. A blood count showed red cells, 5,900,000; Hb, 116%; C.I., 0.99; white cells, 11,000 (polymorphs 80%, lymphocytes 13.3%, monocytes 6.7%); E.S.R., 17 mm. per hour (Wintrobe). The temperature and pulse remained normal during her 10 days' stay in hospital.

Through a small incision 8 oz. (230 ml.) of watery pus containing greyish-white shreds was evacuated. The cavity was 3 in. (7.5 cm.) in diameter, and was situated in the mass of the adductor muscles. The body and inferior ramus of the pubis could be felt and there was no obvious sequestrum. The wound was sutured without drainage. Acid-fast alcohol-fast bacilli resembling tubercle bacilli were seen in stains of the pus. Cultures for the selective isolation of tubercle bacilli were positive.

A 90-day course of streptomycin and *para*-aminosalicylic acid was instituted and the patient was sent home to bed. The wound healed by primary intention in the normal time, and showed firm scar formation after three months. Further *x*-ray films at this stage showed the area of translucency in the pubic bone to be reossifying.

Comment

It is of interest that the abscess fluid had tracked down the leg inside the sheaths of the adductor brevis and longus muscles, the origin of these muscles on the pubic bone coinciding with the situation of the abscess. The fluid tension inside the abscess masked the clinical features, as the "tumour" felt solid, did not fluctuate, and was not tender.

The radiological appearance of the lesion showed a patchy area of bone destruction, with no attempt at any bone formation. The absence of any bone reaction to the local tuberculous process would seem surprising in a young patient in such good general health. This type of *x*-ray appearance resembles that seen in osteitis pubis following prostatectomy, which also leads to gross rarefaction of the bone, giving a "moth-eaten" appearance (Mortensen, 1951). Osteitis pubis is a self-limiting condition, characterized by widespread decalcification and then normal healing, with no sequestrum formation (Hoch and Kurtz, 1951). This seems similar to the case presented here. The aetiology of osteitis pubis is still doubtful, although various factors have been described. May it not be that the pubic bone reacts in a similar way to lesions of different types—trauma, infection, ischaemia, tuberculosis, etc.?

I should like to thank Mr. R. K. Debenham for permission to publish this case, and Mr. T. S. Donovan for his advice about its management.

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References

Clavel, M. (1951). *Chirurg. Apar. locomotor*, **8**, 149.
Fical, A. (1949). *Minerva chir. (Torino)*, **4**, 457.
Girdlestone, G. R., and Somerville, E. W. (1952). *Tuberculosis of Bone and Joint*, 2nd ed. Oxford Univ. Press, London.
Hoch, E. F., and Kurtz, K. A. (1951). *J. Urol.*, **65**, 419.
Mallo, E. (1947). *Rev. med. Hosp. ital. La Plata*, **5**, 246.
Mortensen, H. (1951). *J. Urol.*, **66**, 412.

Sacro-iliac Strain

The wave of popularity for the "disk lesion" as the cause of low backache with associated referred pain in the leg has tended to submerge other diagnostic labels that were previously in favour. The term "sacro-iliac strain," used to define pain of mechanical origin arising in the tissues of the sacro-iliac joint, has in my opinion suffered an undeserved eclipse, an opinion which has been notably reinforced by personal experience of the symptoms thereof on three separate occasions.

For the diagnostician no teaching can compare to that of personal experience. I am therefore in the fortunate position of being able to recognize without difficulty those of my patients who are suffering from the same condition, and may also, I feel, be able to help others to sort out this particular cause of backache from the rather confused clinical picture as it presents itself to the clinician.

On the first occasion I noticed difficulty in standing upright on emerging from a bathe in a rather rough sea. On attempting to do so I experienced pain in the region of the left sacro-iliac joint. By the next morning I felt stiff in this region, with pain, particularly on attempting any twisting movement, local tenderness over the posterior ligament of the joint, and referred pain to the upper and outer aspect of the thigh and in the groin. The following day I was manipulated by my chief assistant. The movement comprised a rotation of the pelvis to the right, the left iliac crest being also thrust downwards at the end of the movement. At this point I felt a "thud" in the region of the left sacro-iliac joint, as if something had "snapped" rather than clicked home. The pain was immediately relieved.

A few years later, some hours after digging a trench and throwing out the earth to the right, I felt an ache in the same spot. This became worse during the next few days and referred pain of the same distribution developed. I then had a further manipulation. Although I again felt a "thud" as if something was reseating itself, I was disappointed to find the pain still present. However, it disappeared during the course of the next twenty-four hours.

On the third occasion the pain came on gradually without any specific injury, though I had been indulging in various physical activities. After about three weeks I got tired of it and had another manipulation. For the first time this was a little painful, and there was no satisfying "thud." The pain was not relieved but gradually subsided before I got to the point of having a "proper" manipulation under thiopentone.

Comment

As the result of these experiences I am personally convinced (1) that there is such a condition as a sacro-iliac subluxation, this being probably a slight rotatory displacement of the joint surfaces, the sacrum being twisted downwards and forwards on the affected side. The feeling of something reseating itself when the pelvis was forcibly rotated in the same direction, associated with an immediate feeling of relief of tension, was quite unmistakable. (2) That there is also a condition of sacro-iliac strain which results from strain on the ligamentous tissues with, subsequently, a reflex inflammatory reaction; and that this may occur as a result of some unaccustomed activity without there necessarily being any actual subluxation of the joint. (3) That, from observations on patients, sacro-iliac strain may also be secondary to disk lesions in the lower lumbar region complicating the clinical picture produced by the disk lesion itself. Finally, the following clinical signs and symptoms will help to distinguish lesions of the sacro-iliac joints from other causes of low back pain. (1) The pain is produced or intensified by rotatory movements, flexion and extension being free and painless unless forced. (Whereas in disk lesions it is flexion and extension that causes pain, rotation being painless.) (2) Referred pain when present will be in the upper and lateral aspect of the buttock and thigh and into the groin. No lesion of the lower lumbar spine can produce referred pain in the groin. (3) There will be tenderness over the posterior ligament of the joint—that is to say, one finger-breadth below and medial to the posterior inferior spine. (4) There will be no limitation of straight-leg raising, although this may cause slight pain at extremes, and no loss of reflexes or other evidence of disturbed function of the peripheral nerves.

In conclusion, I would point out that my own reaction to treatment was typical of the average case—dramatic cure after the first manipulation, delayed relief after the second, and no relief with the third; though there is the consolation that the condition is, I think, and hope, unknown in the elderly.

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Reviews

CLINICAL PATHOLOGY IN GENERAL PRACTICE

Clinical Pathology in General Practice. Specially commissioned articles from the *British Medical Journal*. October, 1953–July, 1954. (Pp. 321+ix; illustrated. 21s.) London: British Medical Association. 1955.

"This century has seen enormous progress in the application of pathology to the elucidation of clinical problems"; with this sentence S. P. Bedson opens the first article. There is no doubt that a high standard of clinical practice depends more on the quality of the pathological services than upon anything else. Indeed, faced with the problem of raising the level of clinical practice in an area, probably the best initial step is to introduce an adequate number of clinical pathologists provided with ample laboratory facilities. Their influence would permeate all branches of clinical practice. Now, that is not quite the same thing as providing laboratory aids for general practitioners. It is wisely emphasized in this admirable book that the fullest contribution of the clinical pathologist to general practice is the provision of a consultant service. Any idea that the National Health Service should provide laboratory tests for general practitioners as a "demand service" without the intervention of the pathologist as a helping, consenting partner merely shows ignorance of the conditions of modern clinical practice. Even the hospital clinician, constantly engaged in the major problems of organic disease and often possessed of a considerable background of personal laboratory experience, is constantly in need of the advice, as well as the technical skills, of the haematologist, bacteriologist, biochemist, etc. How much more is the general practitioner, less preoccupied with gross organic disease, in need of the consultative help of the clinical pathologist.

A prerequisite for success in this process is that not only should the pathologist have some knowledge of clinical practice but the clinician should have some knowledge of laboratory practice. It is in helping the clinician thus that this compendium of clinical pathology in general practice achieves a lucid, eminently practical, and in several places even enthralling account of modern applied pathology. The editor is to be congratulated in his selection of authors. Of adverse criticism I have none; to attempt to appraise the degrees of excellence would be invidious, and I will limit myself to only one specific comment. Dr. Paul Fourman's article on the "Electrolyte Changes in the Blood" is so excellent in its clear exposition of so much that can so readily baffle that it was with a keen sense of disappointment that I found it was not followed by a second article by him describing the application of these principles to several standard problems.

Personally I have learnt much with pleasure from this book, and I urge all to buy it. Many, I know, will have an untidy file of these articles collected as they appeared; let them please their wives by now replacing this with a neat volume.

W. Melville Arnott.

FRACTURES IN THE YOUNG

Fractures in Children. By Walter Putnam Blount, A.B., M.D., F.A.C.S. (Pp. 279+x; illustrated. 72s. 6d.). London: Baillière, Tindall and Cox. 1955.

This excellent book treats of a subject not generally expounded so fully or so clearly: the special mechanics, bodily reactions, and treatment of fractures occurring during the period of growth. Too many textbooks are apt to leave the student with the impression, on which action is not infrequently undertaken, that a fracture of the femur or the bones of the forearm in a child is simply a miniature version of what it would be in an adult. Dr. Blount has obviously an immense experience of fractures in the young, generously supplied by the continual improvements in the speed of motor-cars, together with sympathy for the feelings of the patient as well as regard for the laws of mechanics and physiology.

He makes many important points which, though not revolutionary, are frequently neglected. Some of the more conventional of his readers may be slightly shocked when he emphasizes them by adding to uncommonly good radiographs, photographs, and drawings several cartoons in the style of the pervading comic strip. My own feeling is that no way of hammering home some of the lessons he teaches should be neglected. These crude presentations—of a surgeon with an ass's head congratulating himself on a radiograph while a child with an early ischaemia howls in the background, or of a powerful physiotherapist with a similar cranium treating a stiff elbow—may possibly influence some on whom a single unemphatic sentence would have no effect.

It is good to see the Hamilton Russell traction, unexcelled in many cases of fractured femur, strongly recommended. Further teaching agreeing with the principles of that earlier master is that a slight overlap is often the best possible position for a fracture of a long bone, and the already-mentioned principle that a stiff elbow after a fracture in the neighbourhood should be left strictly alone. Other points are that in the absence of interference, either by operation or by excessive traction, non-union in normal children is practically unknown; that soft, growing bones take screws and plates extremely badly; that angulation, particularly if in the same plane as the action of neighbouring hinge joints, has a strong tendency to correct itself; and that it is possible to cause troublesome lengthening in children's bones of a kind unknown in adults.

In subsequent editions it might be an improvement to have more description of birth fractures of the femur, so alarming in radiographs and so incredible in spontaneous reconstruction. One would also like to know more of what a surgeon of this quality thinks about the difficult and complicated subject of congenital fractures, pseudarthroses, and bends of the long bones.

Denis Browne.

THE PROCESS OF GROWTH

Dynamics of Growth Processes. Edited by Edgar J. Boell. (Pp. 304+vii; illustrated. $7.50.) Princeton: University Press. 1954.

Contributions to the symposia of the Society for the Study of Development and Growth have usually appeared as supplements to the journal *Growth*. The *Dynamics of Growth Processes* presents for the first time in book form papers given at a symposium held in July, 1952. The fact that the book was not published until 1954 and has only reached the reviewer three years after the meeting was held calls attention once more to the difficulties which nowadays prevent rapid publication.

The proceedings of so many symposia are now being published in extended and often expensive form that perhaps the first test which any new volume must pass to justify its existence—even if belated—is whether the contributions are authoritative surveys deserving permanent record or are in the nature of working reports intended mainly for the benefit of the participants of the symposium or to elicit criticism and comment from them, and which will probably be incorporated in other publications. There is no doubt that the material in this book justifies separate publication and that it has lost little from the delay. The papers cover an enormous range of topics, from the replication of protoplasmic units in viruses via an analysis of factors governing growth of bacteria to cellular and tissue growth in animals. Growth and differentiation in plant tissues are given equal emphasis. Finally the growth of individuals is left behind and the growth of populations is considered.

The spread of subject matter is so wide that even the most omnivorous individual reader will have difficulty in digesting all the information and views put before him. He will still find it worth while to dip into chapters which at first glance may seem a little remote from his interests. It is invidious to select any one paper for attention, but it

may be thought fair, in a review in a medical journal, to mention Greulich's, the most directly medical of the papers, lest it go unnoticed. Greulich emphasizes the inadequacies of ordinary height and weight tables as indices of normal development, and puts forward the suggestion that the study of an *x*-ray film of the hand and wrist provides a suitable index of maturity independent of size. He shows how such radiographs can help to predict the time of onset of the menarche or the time of epiphysial closure and hence the final height of patients suffering from disorders of growth.

Each paper is given a good bibliography, and the whole book is well presented. Almost all traces of a symposium atmosphere have gone, and there are only very occasional footnotes discussing points which were raised in what, I expect, were long and interesting discussions. The lack of a report of this part of the symposium, and the title (can growth ever be a static process ?), are the only things about the book to be criticized.

P. L. Krohn.

ANGINA PECTORIS

Angina Pectoris. By Professor Dr. W. H. Hauss. Foreword by Professor Dr. Ferdinand Hoff. (Pp. 394+xii; illustrated. D.M. 59.40.) Stuttgart: Georg Thieme Verlag. 1954.

This book on angina pectoris, dealing with the origin, recognition, assessment, and management of attacks of cardiac pain, provides a full study of the subject from the minor vasomotor disturbance to full infarction. To start with, there is a historical chapter. The morbid anatomy is then described, and then the morbid physiology, and then the clinical aspects, so far as these three topics are concerned in the causation of the pain. The figures for the clinic in Frankfurt show an increase in cardiac infarct from 0.3% of the total intake in 1937 to 2.38% in 1953. There was a striking fall in the figures in the years 1944 and 1945.

In the section on infarction the cardiograms are numerous and adequate. The Nehb triangle is usually shown and takes the place of the unipolar limb leads. The not uncommon infarction without pain hardly finds place for discussion from the point of view of this book. The usual measures to reduce coagulation of the blood are described. For collapse the suprarenal hormone and salt are recommended. Strophanthin is suggested in severe collapse to counteract the overload of the measures against the collapse, such as bandaging the limbs, blood transfusion, and so forth. In the discussion of treatment a good many drugs are mentioned, but more indication for their selection would be useful. This is altogether a sound and competent presentation of a "disease which, in our age, plagued with strain, haste, restlessness and mental depression, belongs to the burning problems of medicine," as the preface puts it.

Terence East.

HANDBOOK OF MEDICINE

Manuel de Médecine. By Henri Péquignot. (Pp. 729; 3,200 fr.) Paris: Masson et Cie. 1955.

The assiduous student, in memorizing a lot of facts, often fails to see his subject in perspective. As the author of this handbook of medicine says, his fragments of knowledge recall the ruins of Palmyra, finely worked sculptures set in the midst of a desert. The student of medicine in France faces particular difficulties because he earns the privilege of working in a hospital only by passing a competitive examination, the *externat*, and until then he does his learning without getting very near the patient. This handbook is meant to provide a background for more detailed studies. It is a summary rather than an introduction, something the student is more likely to fall back on in the hurried weeks before an examination rather than turn to at the beginning of his studies. It is well laid out and clearly written and modern in its outlook. It gives proper weight to the social factors in disease, and emphasizes developments such as catheterization studies and steroid assays, revealing a change in the emphasis of teaching. It is a pity this is also reflected in a change in the language. Many English words now enter into French medical writing, such as "intercurrent," "standard," and "test," and form part of a new jargon, as in "*le test se positive.*" Much that is traditional and outworn has been discarded, but also some that should still stand, and from the student's point of view there are some worrying omissions in descriptions of symptoms and signs. But the vivid names of the classical signs survive—for example, "*signe du glaçon*," the sign of a floating piece of ice, for feeling the liver through a collection of ascitic fluid. The English reader will find many unfamiliar eponyms; for most of them the origin is unfortunately not given.

This is a remarkable compendium for one man to have written; but, as he says, a student should not use it as his only source.

Paul Fourman.

INADEQUATE MEN

Three Men: An Experiment in the Biography of Emotion. By Jean Evans. Introduction by Gordon W. Allport. (Pp. 297+xviii. 15s.) London: Victor Gollancz Ltd. 1954.

"Above all, good case-writing must absorb the reader's attention." So writes Professor Allport in his introduction to this history of three misfits. Case-writing seldom provides absorbing reading, and so the unusual attempt to present the social ups and downs of maladjusted individuals, in the form of a novel, is worthy of praise. Interpretation is reduced almost to zero and the reader is left to form his own conclusions, presumably on the possibilities and opportunities of social work among those who seem incapable of helping themselves.

The three "cases" have one feature in common—a lack of prudence and an inability to profit by experience. It would seem unlikely that the most devoted social worker backed up by an enlightened public authority and an idealistic police force could have made anything of these inadequate men. The setting is in the United States, and consequently many of the allusions will be lost upon the reader unfamiliar with the medical and social institutions in that country. Despite this, the detailed records give a glimpse of American life not often available.

The book, by intent, does not lead up to any conclusion; it has no lesson to teach; it does not attempt to prove anything. The presentation of facts, in however interesting a manner, is apt to leave the reader wondering what the author had in mind. But this is not disclosed. Exasperating though this may be to the student, it is perhaps a relief to the experienced social worker. To see an accomplished colleague at work can be stimulating, and there is no doubt about the skill of Miss Jean Evans as observer and narrator.

The book was published in the United States in 1950, and the present edition has been brought up to date with further details of the three leading characters.

E. A. Bennet.

CEREBROSPINAL FLUID

The Cerebrospinal Fluid. By S. Lups, M.D., and A. M. F. H. Haan, M.D. Introduction by Pearce Bailey, M.D. (Pp. 350+xv; illustrated. 52s. 6d.) Amsterdam, Houston, New York, London: Elsevier Publishing Co. 1954.

This book follows orthodox lines in its description of the cerebrospinal fluid and should prove useful for reference. There are satisfactory sections on anatomical and physiological aspects and on methods of obtaining cerebrospinal fluid, and a long section on methods of examining it, particular attention being given to the various types of colloidal reaction. The results of these reactions are expressed as graphs instead of by the numerical method commonly used in Britain. An account of the C.S.F. changes which may occur in various diseases occupies more than half of the book and is based on the authors' extensive experience, with somewhat infrequent reference to other workers' findings. There is an unfortunate misstatement in the publishers' blurb which describes this as "the first book to be devoted to the cerebrospinal fluid," when in fact a number of books on the subject have appeared since Mestrezat's classic monograph of 1912.

J. W. Aldren Turner.

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CONTRAINDICATIONS TO THIOPENTONE ANAESTHESIA

Twenty years have elapsed since the introduction of thiopentone sodium as an anaesthetic, and the administration of it has increased to such an extent that it is now used for induction or maintenance in the majority of anaesthetics given in Britain. As a result of this experience certain contraindications have come to be recognized, though opinions differ on which of them should be regarded as absolute, the number perhaps diminishing with the experience of the administrator.

The contraindications fall into two classes: first, those imposed by the circumstances of the administration, and, secondly, those dictated by the condition of the patient. Heading the former group is lack of experience by the anaesthetist, which many consider the strongest contraindication of all. Another is that out-patients who must return home unaccompanied should never receive thiopentone. Both these points have been the subject of litigation in recent years. There is general agreement that only in exceptional circumstances should an operator acting alone also function as anaesthetist. Despite the ease of its administration, thiopentone is highly unsuitable for use in such a situation, constant vigilance over the patient's respiration being essential for safety. This hazard of respiratory obstruction or failure further implies that thiopentone should not be given in the absence of apparatus for inflating the lungs with oxygen, or at least air, and for establishing a clear airway (intubation may on occasion be necessary). For similar reasons induction of thiopentone anaesthesia in the patient's room or ward before taking him to the operating-theatre is unwise.

The patient may be an unsuitable subject, for lack of superficial veins or collapsed veins may make venepuncture impossible. The difficulty of intravenous injection is the main reason for avoiding the administration of thiopentone to children (although rectal thiopentone is a valuable premedicating agent for them); moreover, most children do not take kindly to injections. But when venepuncture can be performed easily thiopentone may be given provided the dosage is reduced in accordance with the size of the child. The greatest care in venepuncture is always necessary; damage to nerves has been reported, and extravenous injection of the usual 5% solution of thiopentone may lead to tissue necrosis. Intra-arterial injection is a disaster, for gangrene of the hand almost invariably follows. These necrotizing effects appear to be much less severe for 2½% thiopentone solutions, and to reduce the risks perhaps this weaker strength should be adopted for routine use in Britain as it has been in the U.S.A.

Despite the tranquil induction which it usually affords, thiopentone must not be administered to a patient with a full stomach: the usual care in preparation for a general anaesthetic should be taken. In cases of intestinal obstruction regurgitation and aspiration are major hazards, and, after evacuation of the stomach by means of a tube, induction of anaesthesia with thiopentone and succinylcholine should be followed by immediate insertion of a cuffed endotracheal tube. When respiratory obstruction is present, the induction of anaesthesia with thiopentone is absolutely contraindicated until after the obstruction has been relieved—for example, by intubation under local analgesia. A clear airway must similarly be guaranteed during emergence. Cases falling into this group include laryngeal oedema (which may not always be obvious, as in cases of flash burns or during pregnancy toxaemia) and Ludwig's angina and similar phlegmons in the neck. In operations on the upper air passages intravenous anaesthetics may seem convenient and are easily administered, but thiopentone and other such agents are contraindicated unless the airway is guarded—for instance, by intubation and packing—against inundation by blood, foreign bodies, and so on. If thus administered in nose and throat operations the dosage of thiopentone should be restricted in order to ensure prompt recovery. For peroral endoscopy thiopentone alone is inexpedient, since grave anoxia may result from laryngeal spasm. Thiopentone should not be given to patients with gross dyspnoea due to disease of the heart or lungs or with constrictive pericarditis, since it can precipitate acute circulatory failure. In shock and dehydration, severe anaemia, and toxaemia the dosage of thiopentone must be very greatly reduced; likewise when elimination is retarded—for example, in severe renal or hepatic disease or myxoedema.

In obstetrics the administration of thiopentone generally has been discouraged, because depression of the baby's respiration is a possible sequel. Despite this, a small induction dose (less than 0.25 g.), accompanied by succinylcholine and followed at once by insertion of a cuffed endotracheal tube, has been advocated as one means of overcoming the grave

hazard of regurgitation and aspiration of vomitus, an ever-present danger of anaesthesia in parturient women. For external version thiopentone alone is unsuitable, because the relaxation is inadequate for the procedure. In severe uraemia and in three rare conditions—Addison's disease, porphyria, and dystrophia myotonia—thiopentone has adverse effects and is contraindicated. Finally, it is worth noting that with thiopentone alone relaxation—for example, for laparotomy—is not profound, and resistant subjects may be difficult to subdue for even minor procedures. Pushing up the dose to attain relaxation leads to a high degree of tissue saturation, so that recovery is delayed and depression of respiration may result. The administration of thiopentone alone in this manner is therefore inadvisable.

CHEMOTHERAPY OF CANCER

Since the conclusion of the second world war some advances have been made in the chemotherapy of cancer. Largely as a result of studying chemical warfare agents, it was discovered that mustard gas (di-2-chloroethyl sulphide) and a number of nitrogen mustards (di-2-chloroethylamines) and their derivatives had systemic effects on blood-forming tissues. This discovery stimulated researches into the pharmacological and biological action of a number of the chloroethylamines.

Cytological studies showed that many of the nitrogen mustards have a toxic action on cells in a state of active proliferation. In low doses these compounds arrest mitosis, but at higher concentrations they induce chromosome fragmentation and other abnormalities in the dividing cancer cells. Because these nuclear changes are characteristics of nitrogen mustards and are similar to those induced by *x* rays, these compounds have been called "radiomimetic." This observation was of particular interest because here was a drug capable of inhibiting cell division in tumours without apparently unduly affecting normal tissue cells. This mode of action of the nitrogen mustards is not fully understood chemically, but is thought to concern enzyme inactivation.

After research workers had shown, chiefly in Britain and the United States, that nitrogen mustards have an inhibitory effect on the growth of various tumours and leukaemias in experimental animals, their clinical application was given serious consideration. A. Haddow and his colleagues[1] were among the first workers in this field to realize that in order to administer compounds with greater clinical safety it would first be necessary to obtain chloroethylamines of a much lower toxicity. They prepared a series of derivatives of aromatic amines, among them being 2-di-(2′-chloroethyl)aminonaphthalene, which is commonly known as R. 48 (CB 1048). This drug had the advantage of being administered orally. The clinical trials were first reported by W. B. Matthews.[2] Although the responses in cases of Hodgkin's disease were disappointing, remissions were achieved in cases of chronic myeloid and lymphatic leukaemias. The toxic symptoms were relatively mild and the gastric disturbances were not severe. Looking for further structural changes, Haddow, W. C. J. Ross, and others[3 4] developed derivatives of aromatic nitrogen mustards with acid side-chains (for example, CB 1348). Haddow, F. Bergel, and J. A. Stock[5 6] extended this research to compounds related to natural α-amino-acids (CB 3007). Haddow and G. M. Timmis,[7] on the other hand, modified the nitrogen mustard group by introducing sulphonic ester groups. Further simplification led to a series of sulphonic acid esters which were derived from simple straight-chain polymethylene compounds. One of these substances, a chain of four carbon atoms between the two methane sulphonoxy groups, CB 2041, showed optimal effects under experimental conditions and was then introduced under the name of "myleran." Later D. A. G. Galton and M. Till,[8] who supervised the clinical trials of this compound at the Royal Cancer Hospital, found it to be an effective palliative in cases of chronic myeloid leukaemia. Myleran was furthermore found to be a satisfactory substitute for radiotherapy, and when given in therapeutic doses it depressed myelopoiesis without seriously affecting other haemopoietic elements.

Meanwhile simultaneous investigations into drugs related chemically to the active nitrogen mustards, which also had the advantage of being cross-linking agents, known as the ethylenimines, were undertaken in London by Haddow,[9] in Manchester by F. L. Rose, J. A. Hendry, and A. Walpole,[10] and in New York by J. H. Burchenal and his colleagues.[11] These compounds were found to inhibit tumour growth, and one of them, triethylene-melamine (T.E.M.), is found to give benefit in selected cases of lymphosarcoma, Hodgkin's disease, and chronic myeloid and lymphatic leukaemia. Two interesting papers have recently appeared by C. L. Bateman and N. J. Smith *et al.* in the United States.[12 13] The former treated

[1] Haddow, A., *et al.*, *Nature* (*Lond.*), 1948, **162**, 824.
[2] Matthews, W. B., *Lancet*, 1950, **1**, 896.
[3] Haddow, A., *et al.*, *A.R. Brit. Emp. Cancer Campgn*, 1952, **30**, 25.
[4] Everett, J. L., *et al.*, *J. chem. Soc.*, 1953, p. 2386.
[5] Haddow, A., *et al.*, *A.R. Brit. Emp. Cancer Campgn*, 1953, **31**, 6.
[6] Bergel, F., and Stock, J. A., *J. chem. Soc.*, 1954, p. 2409.
[7] Haddow, A., and Timmis, G. M., *Acta Un int. Cancr*, 1951, **7**, 469.
[8] Galton, D. A. G., and Till, M., *Lancet*, 1955, **1**, 425.
[9] Haddow, A., *A.R. Brit. Emp. Cancer Campgn*, 1950, **28**, 56.
[10] Rose, F. L., *et al.*, *Nature* (*Lond.*), 1950, **165**, 993.
[11] Burchenal, J. H., *et al.*, *Arch. Biochem.*, 1950, **26**, 321.
[12] Bateman, J. C., *New Engl. J. Med.*, 1955, **252**, 879.
[13] Smith, N. J., *et al.*, *J. Pediat.*, 1955, **45**, 493.

91 patients suffering from a variety of advanced carcinomas with triethylene thiophosphoramide (thio-T.E.P.A.). Clinical improvement was observed in 80% of the patients; breast and ovarian tumours appeared to be particularly sensitive to this drug. Smith and his colleagues, using the same compound, treated 21 children under the age of 15 years suffering from leukaemia, lymphosarcoma, or Hodgkin's disease. Fourteen died during treatment. No beneficial effect was exerted in cases of acute leukaemia; temporary relief was obtained in cases of lymphosarcoma, Hodgkin's disease, and chronic leukaemia. Clinical experience has indicated that most of the ethylenimine derivatives in comparison with the aliphatic nitrogen mustards cause fewer side reactions, but they may induce bone-marrow depressions that occur later than with the nitrogen mustards and in some cases are irreversible. Therefore, in order to avoid this serious complication, therapy must be guided by careful clinical evaluation.

Chemotherapy of cancer at present is still mainly a palliative procedure in advanced cases. None of the drugs yet given can be regarded as curative, but the fact that temporary remissions without any serious side effects can be attained by nitrogen mustards and their derivatives should be regarded as a milestone in cancer research.

MENTAL DEFECTIVES IN HOSPITAL

Public opinion is understandably sensitive about the compulsory detention of mental defectives in hospitals. Allegations, however ill-founded, that a patient has been wrongly certified as mentally defective or wrongly detained in a hospital can damage the reputation of the mental health service generally, and it is worth recalling the precautions which have to be taken to avoid such a disastrous mistake. In the first place the ascertainment and certification of a mentally defective patient are for the most part carried out by experienced and knowledgeable officers of the local health authority. Then, on arrival at the hospital, the patient must be examined by a consultant, who may refuse to accept him as certifiably defective—a rare event, but it does happen. The original order admitting the patient to hospital has force for a year, but may be renewed for one year and then for five-year periods. For this purpose there are statutory times when the patient appears before the "visitors" for consideration of his future. These visitors are one or more specially selected justices who, accompanied by a doctor, visit before the end of each quarter to see every patient whose order is about to expire. They see the patient, they have a reliable report on the home conditions, and they receive any other information they may wish for. On this examination the justices form their opinion and give to the Board of Control their recommendation that the order should or should not be renewed. At the same time the medical officer, usually a consultant, submits to the Board his own statement and certificate on the patient's need for further detention or otherwise. Only the Board of Control has the power to renew the order or to discharge it. In addition to these periodical reviews of the case there is a special reassessment when the patient reaches the age of 21. On this occasion the justices have the power actually to order discharge, and the relations have the right to be present and to see the justices.

Such in the main are the formal provisions for keeping each case in review, but it is not only or mainly by these means that patients return to life in the community. The wards are visited daily by the physicians on the hospital staff, at frequent intervals by the medical superintendent, monthly by two members of the committee of management, and at least annually by the inspectors of the Board of Control. On all these occasions a patient may speak for himself or may ask for an interview: he may always write unhindered to the Board of Control and to certain other people, and his friends and relations can do the same. It is by action initiated in this way, either from the patient's side or from the medical side in the course of regular consideration of each case, that recommendations go to the Board and lead to most discharges.

These facts are not always known to those who complain that it is too difficult for a patient to obtain freedom from his order and who think that the machine is inadequate or that those who operate it are obstructive. Even so it is inevitable that compulsory detention will sometimes make the patient bitter and morose and his relatives suspicious of the hospital authorities. The necessity for the formal certification of every patient has often been questioned, and the British Medical Association[1] and the National Association for Mental Health[2] have now recommended to the Royal Commission on the Law relating to Mental Illness and Mental Deficiency that, whenever possible, a defective patient should come under care in a voluntary category or by the voluntary action of his relations or friends. Only when these methods cannot be used and a justice of the peace has been convinced that detention is necessary in the interests of the patient or for the protection of the public should

[1] Minutes of Evidence on the Law relating to Mental Illness and Mental Deficiency, No. 26, H.M.S.O., London. See also *British Medical Journal Supplement*, May 7, 1955, p. 211.

[2] Memorandum of Evidence on Mental Deficiency prepared by the National Association for Mental Health, 39, Queen Anne Street, London, W.1.

an order be made. In order to provide full legal safeguards the National Association for Mental Health also recommends that the proceedings should be conducted before two magistrates sitting together, that the testimony and evidence should be sworn, and that there should be right of appeal against the magistrate's decision. Patients in the voluntary or placed categories should, broadly speaking, leave the hospital by the same door through which they entered—that is to say, at the wish of themselves or their friends. The B.M.A. also made several recommendations concerning the certified patient. One of the two certifying doctors should be a consultant experienced in mental deficiency. This should eliminate the slight risk of an unsuitable patient being recommended for admission, and at the same time it should protect some patients from being deprived of the form of treatment which they need—as sometimes happens through failure to recognize the less obvious defective. Each case should be formally reconsidered at the intervals of 1, 1, 3, and 5 years—once more in the early years than at present—and the relatives should have the right to be present, or to be represented, and to produce independent psychiatric opinion. The purpose of these suggestions is to make it abundantly plain that when a patient asks for discharge, either directly or through his relatives, the request will be considered fully and fairly. At each visit the justices should have the power to order discharge if so advised by the medical officer. They would, of course, retain the right to make their own recommendations to this effect even if the doctors were not in agreement. In such cases it is left to the Board of Control to decide. Finally, the B.M.A. recommends that the Board of Control should be retained in a position of independence and strengthened in numbers so that it can take a more active part in the investigation of difficult and disputed cases.

WHEAT-FREE DIET IN STEATORRHOEA

The removal of starches from the diet of children suffering from coeliac disease has long been known as an effective method of treatment.[1–5] Comparable clinical success has also been claimed for the banana diet[6] and for the vegetable and fruit diet of G. Fanconi.[7] The important observation of W. K. Dicke[8] and the subsequent studies of H. A. Weyers and J. H. van de Kamer[9 10] have shown that the benefits of these diets lay in the exclusion of wheat flour, and that, provided the gluten fraction of wheat and rye flour was omitted, starch could be fed without ill effect. These observations have been fully confirmed by English workers.[11 12] The means by which gluten exerts its harmful effects remain unexplained. C. M. Anderson and her colleagues[11] suggest that the absorption defect may possibly be due to excessive mucus secretion or lack of intestinal motility, or even to a combination of both factors. A. C. Frazer[13] enlarged on this and suggested an allergic reaction of the intestinal wall to gluten. The Dutch workers, on the other hand, concluded that wheat or rye probably precipitated a disturbance in fat metabolism, thereby bringing on the symptoms of disease already latent and presumably congenital in origin.

The theoretical aspect is, however, less important than the great therapeutic advance that has resulted in the treatment of coeliac disease in children, and it is not surprising that the gluten-free diet has been tried empirically in the treatment of adults with idiopathic steatorrhoea, non-tropical sprue, or the sprue syndrome. Ruffin and his colleagues in the U.S.A. have reported three patients so treated with dramatic and gratifying success. C. McIver[14] and Anderson and her colleagues[15] in England and A. J. Ch. Haex and J. B. Lips[16] in Holland have all reported successful results. But not all patients with non-tropical sprue respond satisfactorily. Perhaps 10% show immediate improvement and another 30 to 40% may have to remain on a gluten-free diet for up to eight months before a clinical cure can be claimed. Even then, the reintroduction of gluten-containing foods may cause prompt relapse. There is, however, no way of finding out in advance which patients will respond completely, partially, or not at all to the exclusion of gluten. This is unfortunate, because, as Professor A. C. Frazer points out in the paper published in the opening pages of this issue, a wide range of common foodstuffs must be excluded from the diet, "since wheat flour is widely used in infant foods, pudding mixtures, sauces, soups, confectionery, and custard powders, as well as in bread, cakes, and biscuits." Of necessity, therefore, the patient's co-operation is essential for successful therapy. Most physicians who have treated a number of adult patients with idiopathic steatorrhoea will have seen some who, though not quite normal haematologically and excreting a slight excess of fat in their stools, nevertheless claim that they have never felt better since they restricted fat in their diet and are able to lead an energetic life. A gluten-free diet to such patients may be a severe and perhaps unnecessary burden. It is also possible, if Weyers and van de Kamer[9 10] are right, that at some phase of the disorder the patient may tolerate gluten, while at other times he may react to it vigorously. Even so, the gluten-free diet has opened the way for

[1] Howland, J., *Trans. Amer. pediat. Soc.*, 1921, **33**, 11.
[2] Sauer, L. W., *Amer. J. Dis. Child.*, 1925, **29**, 155.
[3] Andersen, D. H., *J. Pediat.*, 1947, **30**, 564.
[4] Sheldon, W., *Arch. Dis. Childh.*, 1949, **24**, 81.
[5] May, C. D., and Lowe, C. U., *Amer. J. Dis. Child.*, 1951, **81**, 81.
[6] Haas, S. V., *J. Pediat.*, 1938, **13**, 390.
[7] Fanconi, G., *Schweiz. med. Wschr.*, 1928, **58**, 739.
[8] Dicke, W. K., *Coeliake*, M.D. thesis, 1950, Utrecht.
[9] Weyers, H. A., and Kamer, J. H. van de. Centr. Inst. Voedingsonderzoek T.N.O. (Utrecht), Publ. 113, 1950.
[10] —— —— *Voeding*, 1953, **14**, 37.
[11] Anderson, C. M., *et al.*, *Lancet*, 1952, **1**, 836.
[12] Sheldon, W., and Lawson, D., ibid., 1952, **2**, 902.
[13] Frazer, A. C., *Acta gastro-ent. belg.*, 1954, **16**, 8, 491.
[14] McIver, C., *Lancet*, 1952, **2**, 1112.
[15] Anderson, C. M., *et al.*, *Gastroenterologia (Basel)*, 1954, **81**, 98.
[16] Haex, A. J. Ch., and Lips, J. B., *Ned. T. Geneesk.*, 1955, **99**, 102.
[17] French, J. M., *Postgrad. Med. J.*, 1955, **31**, 299.
[18] Cooke, W. T., and Brooke, B. N., *Quart. J. Med.*, 1955, **24**, 1.
[19] Gee, S. J., *St. Barth. Hosp. Rep.*, 1888, **24**, 17.

further advances in the treatment of these patients, and it is possible, as J. M. French[17] suggests, that there are other substances which may cause similar reactions.

The gluten-free diet has as yet achieved no success in tropical sprue,[11 15] nor in the group of patients with secondary steatorrhoea of the types detailed elsewhere in this issue by Drs. P. H. Friedlander and V. Gorvy, other than a temporary remission in a patient with enterocolitis reported by W. T. Cooke and B. N. Brooke.[18] As Friedlander and Gorvy point out, some of these secondary cases may be difficult to distinguish from primary idiopathic steatorrhoea. Idiopathic in clinical medicine has always implied that the aetiological factor is as yet unknown, and the group of patients with "gluten-induced enteropathy" can be detached from the rapidly diminishing number of those suffering from the sprue syndrome to whom the terms "idiopathic steatorrhoea" or "non-tropical sprue" should be applied: in this group at least Gee's[19] statement is true, "If the patient be cured at all it must be by diet."

CANCER OF LARYNX

Intrinsic carcinoma of the larynx, unlike extrinsic, has a fairly good prognosis. Laryngeal function remains more or less intact after successful radiotherapy, and this form of treatment is to be preferred to laryngectomy when both methods offer a similar prospect of cure. Moreover, a growth which has failed to respond to radiotherapy may still be amenable to surgical treatment. W. D. Harmer[1] considers that laryngectomy should not be carried out in the early cases, and M. Lederman[2] believes that in the advanced cases radiotherapy can give as good results as surgery. However, most authorities agree that for cases of extensive subglottic involvement surgery offers more benefit than radiotherapy.

C. C. Wang and A. R. O'Donnell[3] have recently recorded the results after five years in a series of 253 patients treated for intrinsic carcinoma of the larynx at the Massachusetts General Hospital from 1931 to 1949 inclusive. Of these, 161 were treated by conventional (200 kV) deep *x*-ray therapy, the remainder by surgery. After radiotherapy alone, 28 of 35 patients (80%) with stage I and 13 of 19 patients (68%) with stage II disease survived five years, while after surgical treatment the figures in the same stages were 13 of 15 patients (87%) and 7 of 12 patients (58%) respectively. Fourteen of 58 patients (24%) in the more advanced stages of the disease, but without lymph-node involvement, were well five years after radiotherapy, while with surgery the figure was 28 of 47 patients (53%). In the still more advanced cases the figures were 29% and 25% for radiotherapy and surgery respectively. Harmer, using the Finzi–Harmer surgical fenestration method of radium needling, reported 87% of patients in stage I and II of the disease surviving five years, but with an operative mortality of 6%. Twenty-six of 71 patients (37%) with more advanced disease in Harmer's series survived five years. Lederman,[4] using teleradium therapy, reported 83% of patients in stage I surviving for five years and 51% in stages I and II taken together. Comparable figures for teleradium therapy have also been reported by F. M. Allchin.[5]

It would seem that there is little to choose between the results of the three methods of radiotherapy—deep *x* rays, fenestration, and teleradium—in the early cases, and this may well be true of teleradium and deep *x*-ray therapy in the later stages also. What of the newer megavoltage therapy, whether by *x* or gamma rays—for example, tele-cobalt therapy? It is as yet too soon to predict whether results will be better. On theoretical grounds they seem unlikely to be, since the essential effect on the cancer cell is the same, and the problems of depth dosage in larynx cancer are easily solved with the less powerful weapons. But megavoltage therapy does have one advantage: because of the peculiarities of the absorption curve in the higher voltage ranges, the effect on the skin is relatively much less, and the patient is accordingly spared the well-known discomforts associated with the more severe skin reactions.

EARLY MIXED FEEDING IN INFANCY

Mixed feeding, which has been customary from birth among most ancient and primitive peoples, went out of fashion in the western world during the nineteenth century because it was believed that babies under six months old had delicate digestions that were unable to cope with complicated diets. The prevalence of lethal gastro-enteritis was attributed to dyspepsia rather than infection and every effort was made to encourage breast-feeding or to humanize cow's milk as a substitute. The latter was modified with great attention to detail on the assumption that small variations in composition were likely to lead to success or failure. Now that gastro-enteritis has largely been conquered, paediatricians have been encouraged to make bolder recommendations for infants' diets. Complicated formulae are seen to be unnecessary, and healthy babies come to no harm when allowed to take as much milk as they want. Some babies, however, get full of milk before their appetite is satisfied, and for them more concentrated feeds are required. It is not usual for the young of other mammals to be fed exclusively on milk for more than a few days, and for human babies it is now becoming fashionable to revert to the traditional method by introducing solids ever earlier. Indeed, mixed feeding is sometimes recommended from the first month of life. In a recent paper B. Gans[1] has related the arguments in favour of

[1] Harmer, W. D., *British Medical Journal*, 1953, **2**, 735.
[2] Lederman, M., *Comptes Rendus des Séances, Congrès de 1947, Société Française d'Otorhino-Laryngologie*, vol. 54, pt. 2, pp. 62–71.
[3] Wang, C. C., and O'Donnell, A. R., *New Engl. J. Med.*, 1955, **252**, 743.
[4] Lederman, M., *Ann. roy. Coll. Surg. Engl.*, 1952, **11**, 47.
[5] Allchin, F. M., in Carling, E. Rock, *et al.*, editors, *British Practice in Radiotherapy*, 1955, p. 245, London.

[1] Gans, B., *Nutrition*, 1955, **9**, 8.

mixed feeding in early infancy and has described his own experience with this method. There has been no evidence that healthy young babies are unable to tolerate starch, meat, vegetables, or other adult foods (suitably sieved), and even babies recovering from illness have been able to digest a full diet; they seem to derive more benefit from a high-protein diet contained in less bulk than from milk alone.

However, before advising mixed feeding for all young babies it is desirable to weigh up the arguments for and against it. The advocates state that babies fed in this way show more vitality, look healthier, tougher, more alert, and are more advanced, and the mothers say that as they require feeding less often and share the food of the rest of the family much time and trouble is saved. These contentions are impossible to assess statistically, but it is probably true to say that the diseases encouraged by a prolonged diet of milk alone, such as iron-deficiency anaemia, scurvy, rickets, and idiopathic hypercalcaemia, are unlikely to occur with mixed feeding provided the diet is properly balanced. On the other hand, the antagonist might raise several objections. These diets cost more and advantage is not taken of the subsidy on milk; the babies do not suck so much and hence lack the emotional satisfaction of it; the more complex the preparation of food, the more likely are pathogenic organisms to be introduced; the sophistication of our modern food may produce substances deleterious to the vulnerable infant in subtle ways; and, lastly, the naturalist might be tempted to point out that the teeth would erupt sooner if solids were intended to be given in the first six months. Furthermore, breast-feeding will presumably tend to cease earlier since the stimulus of sucking is reduced. These considerations should make us pause before advocating mixed feeding for all young babies, but at least the advocates of this method have demonstrated not only its safety but that the restrictions often put on the bottle-fed baby are in need of revision.

HAEMOPHILIA

Haemophilia is a rare disease, its incidence, for example, in one region of Britain being 1 per 35,000 of the population. In contrast to the low incidence is the frequency with which the physician has to deal with the problems of the individual patient in general or hospital practice. The severe haemophiliac may suffer a succession of haemorrhagic emergencies throughout a lifetime of chronic invalidism, and he has not only medical but social problems to face: there are the difficulties of education in childhood and of suitable employment during adult life. Earlier this year Dr. R. G. Macfarlane[1] discussed the treatment of bleeding in haemophilia in his article on "the bleeder," published in this *Journal* as one of the series "Emergencies in General Practice."

The Medical Research Council in 1953 established a Haemophilia Committee, and in collaboration with the Ministry of Health and the Department of Health for Scotland the Council has put a scheme of reference centres into operation with the object of co-ordinating information and of ensuring uniformity of diagnosis. The Council has also published this week a memorandum[2] on "The Diagnosis and Treatment of Haemophilia and its Related Conditions," written on the committee's behalf by Dr. R. G. Macfarlane and Dr. Rosemary Biggs, of the Radcliffe Infirmary, Oxford. This valuable publication, which is designed to help clinicians and pathologists to recognize and differentiate the various coagulation defects, contains a useful technical section describing within reasonable compass the techniques required for accurate diagnosis. The laboratory approach to these disorders is not simple, but the tests are within the capacity of any reasonably equipped pathological service. The cause of a coagulation defect may often be suspected by the clinician, but it is only by laboratory investigation that a clotting abnormality can be finally established and its nature determined.

Haemorrhagic disorders are divided into those in which there is a disturbance of the platelet–capillary system and those with some upset of the coagulation mechanism. The memorandum mentions the disorders of the platelets and capillaries, but does not discuss these at length, being more concerned with the disturbances of blood coagulation and, in particular, with haemophilia and other constitutional deficiencies of the components of the clotting mechanism. These components are prothrombin, factors V and VII, antihaemophilic globulin (missing in haemophilia), Christmas factor (missing in Christmas disease), platelets, and fibrinogen. Prothrombin and factor VII are generally deficient together, as in vitamin K deficiency or during treatment with coumarin products. Fibrinogen deficiency is being reported with increasing frequency as a recently recognized complication of pregnancy.[3]

Deficiencies of prothrombin, factors V and VII, and of fibrinogen cause prolongation of the one-stage prothrombin time by Quick's test. When this test is normal the coagulation defect may be haemophilia, Christmas disease, or due to the presence of a circulating inhibitor. The diagnosis of these is dependent on the thromboplastin generation test. By far the most common of these diseases is haemophilia. Christmas disease is much more of a rarity in the United Kingdom, the ratio of incidence being about 1 to 10 cases of haemophilia.

In the section on treatment the memorandum describes the methods of replacing the deficient coagulation factors, particularly antihaemophilic globulin. The importance of freezing plasma to preserve the antihaemophilic globulin content is mentioned. The authors give advice on the management of bleeding from special sites and in particular discuss the problem of dental extraction in haemophilia; here they stress the necessity for impressing on parents the great importance of conservative dentistry for haemophilic children.

[1] Macfarlane, R. G., *British Medical Journal*, 1955, 1, 1080.
[2] —— and Biggs, R., "The Diagnosis and Treatment of Haemophilia and its Related Conditions," Medical Research Council Memorandum No. 32, 1955, H.M.S.O., London. Price 2s. 6d.
[3] See *British Medical Journal*, 1955, 2, 314.

EMERGENCIES IN GENERAL PRACTICE

THE ACUTE ABDOMEN

II. CAUSES OF ACUTE ABDOMINAL PAIN

BY

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Last week consideration was given to the examination of the patient with acute abdominal illness; in this article some of the causes of acute abdominal pain are considered.

Inflammatory Conditions

Acute appendicitis accounts in all except very small children for a greater number of abdominal emergencies than any other condition, and should be suspected in anyone who has pain in the right side and who has not had the appendix removed. The typical account of central pain moving later to the right iliac fossa is not always obtained, particularly if the patient has had a number of previous attacks; in quite a proportion of cases the diagnosis is overlooked because the appendix is in the pelvis and a rectal examination is not made, for in such cases abdominal tenderness and rigidity may be absent. Apart from pelvic appendicitis it is rare to find acute obstructive inflammation of that organ without some degree of tenderness of the abdominal wall, even early in the attack, and such tenderness in the right lower quadrant in a patient with a furred tongue and recent pain should always be regarded as evidence of appendicitis unless proved otherwise. The thermometer is not a good guide in the diagnosis of acute appendicitis—there is often a little fever, but a severely gangrenous appendix may cause no rise in temperature. It is safer to make an exploratory incision than to overlook acute appendicitis early in the attack.

There should be no delay in coming to a decision about an operation just because no mass is palpable, but the presence of a swelling during the first few days of an attack is of serious import; the swelling may be the distended inflamed appendix itself, but more often it is an abscess of which the omentum forms part of the wall. Thus it is unusual to feel a mass before perforation has occurred and the best time for operation has passed. Perforation of an appendix rarely occurs on the first day of an attack, but the symptoms may be so mild before perforation occurs that the patient ignores them. Sometimes, by the time the doctor is called in, the patient already has a spreading or generalized peritonitis and it is impossible to say precisely in which organ the inflammation has started; such patients should be explored surgically as soon as possible.

Perhaps the next most common acute inflammatory disease is acute cholecystitis, but this occurs in the middle-aged and much more commonly in women than in men; there may be no previous history of gall-bladder disease and the physical signs are usually confined to the upper abdomen. Where there is a palpable swelling it may be the gall-bladder itself which is distended, or it may be a mass of oedematous tissue, omentum, mesocolon, and adjacent organs with the gall-bladder in the centre, with or without a localized abscess; fortunately acute suppurative cholecystitis rarely causes generalized peritonitis, for there is time for protective localizing adhesions to form. In some cases an *x*-ray film may show the presence of one or more opaque gall-stones, but a negative radiograph is not helpful; early operation in an attack of acute cholecystitis in an otherwise healthy patient will often cut down the length of illness by many weeks and in good surgical hands carries no more risk than an interval cholecystectomy.

Acute pancreatitis, which accounts for between 1 and 2% of abdominal emergencies, is still a dangerous disease; the rigidity varies in intensity, but is usually confined to the upper abdomen; the characteristic signs—discoloration in the loin, local swelling, and jaundice—are likely to develop late or not at all; and a confident diagnosis can rarely be made without the help of a raised serum amylase level. The general trend at present is towards conservative treatment, but if any doubt is entertained about the diagnosis laparotomy should be undertaken.

Acute salpingitis of sudden onset is much less common than formerly, but secondary infection of a broad-ligament cyst or hydrosalpinx occurs, and thus the importance of a pelvic examination in patients with acute lower abdominal pain, which may be suprapubic or referred to one or other iliac fossa, is stressed; in many of these patients the inflammation is chronic with acute exacerbations, so that a history of symptoms dating back some months is often obtained and a vaginal discharge is evidence of infection in the genital tract.

Acute diverticulitis of the sigmoid colon may present either with inflammatory or with obstructive symptoms: the tale that it presents as a case of left-sided appendicitis is only partly true, for often perforation and spreading peritonitis may be the first evidence that anything is amiss, while in other cases a localized left iliac or pelvic abscess comes on insidiously and presents as a tender swelling; unfortunately, patients with this disease are often fat and physical examination is difficult. Diverticulitis is rare under the age of 30 and the liability to it increases steadily as age advances; occasionally the acute attacks are accompanied by quite appreciable haemorrhage from the rectum, a point to bear in mind in the differential diagnosis from a growth in the left colon.

Regional ileitis, or Crohn's disease, may similarly present with inflammatory or obstructive symptoms and may be difficult to distinguish from acute appendicitis; a swelling may be present early in the attack, and it is usually more mobile than an appendix abscess and elongated in shape.

In the lower abdomen most of the acute inflammatory lesions require urgent operation in view of the danger of spreading peritonitis; of those that do not require operation, acute enteritis, acute mesenteric adenitis, and tubercular peritonitis should be mentioned. The first two are mainly diseases of children, the third is rarely diagnosed without a laparotomy; the presence of active pulmonary tuberculosis may give a hint to the diagnosis, but it is surprising how this disease in its acute form closely mimics acute appendicitis in both its symptoms and signs.

Acute renal infections may cause some anxiety in diagnosis, for rigidity may make palpation of the kidney difficult, and frequency of micturition may occur in cases of appendicitis or diverticulitis when the inflamed organ is related to the bladder; as a rule, higher temperatures are found in acute pyelonephritis, and examination of the urine for pus cells will probably settle the doubt.

Obstructive Lesions and Colics

The characteristic pain of an obstructive lesion is a colic, and it is usually not difficult to distinguish by their distribution between intestinal, biliary, or renal colic. The main difficulty is in knowing whether intestinal colic is associated with acute organic obstruction or merely with irritation causing excessive peristalsis. Both may be associated with vomiting, but in the absence of organic obstruction diarrhoea rather than constipation is a usual concomitant. The

examination may be most helpful. Palpate the hernial orifices, for strangulated herniae are much the most common cause of acute intestinal obstruction and they are nearly all inguinal or femoral; when a para-umbilical hernia strangulates it is usually because a knuckle of small intestine has slipped into the sac alongside omentum or transverse mesocolon; strangulated obturator hernia is a rarity, and the diagnosis is hardly ever made before operation.

It is important to examine the patient in a good light, as the presence of visible peristalsis is a most valuable physical sign: if scattered peristalsis is present over most of the abdomen there is probably no organic obstruction; if the peristalsis is seen to come and go persistently in the same loop of bowel, then assuredly there is an organic obstruction and operation must not be delayed. Very early and gross distension suggests the occurrence of a volvulus of the sigmoid colon or caecum, but unfortunately many patients with intestinal obstruction are not seen until some distension is present, and this makes the location of any obstruction more difficult; even so, localized distension may be a valuable physical sign, particularly a distended caecum, which in colonic obstruction is usually the first part of the large intestine to become distended even if the site of obstruction is in the left side of the colon. A local mass may also help in the diagnosis; in cases of acute following on subacute obstruction, as, for example, in carcinoma of the colon, the primary tumour is often palpable, but in most cases of acute small intestine obstruction due to intra-abdominal causes, such as bands or internal hernia, no causative swelling can be detected. A vascular lesion of the mesenteric vessels, either thrombosis or embolism, may present as a case of intestinal obstruction; in thrombosis blood is sometimes passed from the rectum, while in cases of embolism the source of the embolus, such as a fibrillating heart, will arouse suspicion.

Of the remaining colics little need be said. Biliary colic does not always show the characteristic distribution and may sometimes be experienced on the left side as much as on the right; in fact, it is rarely confined entirely to the right side; it may be mistaken for the pain of coronary artery disease, but more often the reverse is the case. Urinary colic—renal or ureteric—is much more characteristic and is rarely mistaken for intestinal colic; if suspected, examination of the urine for red cells after centrifugalization may be helpful. These colics do not require urgent operation, and, if confidently diagnosed, antispasmodic and analgesic drugs may be given.

The fact that lead colic still occurs should be borne in mind. It is many years since I have seen a tabetic crisis simulating acute abdominal disease, but a number of patients with acute porphyria have been admitted to hospital as cases of acute intestinal obstruction and the true diagnosis has been suggested only when the dark colour of the urine has been observed.

Perforations

Sudden perforation of a viscus of the alimentary canal into the peritoneal cavity is nearly always due to a peptic ulcer of the stomach or duodenum, but occasionally acute perforation of a carcinoma of the stomach occurs, and mention has already been made of the fact that perforation of the colon may be the first evidence of diverticulitis. The generalized and board-like rigidity of the abdominal muscles, coupled with the dramatic onset, usually leaves little doubt about the diagnosis of a perforated peptic ulcer; occasionally confusion arises with acute pancreatitis, but in this vomiting is likely to be persistent, and when in real doubt a serum amylase estimation will be of value. The other type of perforation which may be overlooked is the leaking duodenal ulcer. A little fluid runs down the right paracolic gutter to the right iliac fossa and then the signs mimic appendicitis; such patients may carry on for a day or two before they call in a doctor, and then at operation the perforation may be found sealed with omentum. It is in just these cases that an *x*-ray picture of the abdomen will be of great value, for if there has been any appreciable escape of their contents from the stomach or duodenum free gas in the peritoneal cavity will be evident. Conservative treatment has a place in the management of some cases of perforation of a peptic ulcer, but if there is any doubt about the diagnosis exploration will be the safest course except in an extremely ill patient.

Torsion

There are not many abdominal organs which undergo torsion, as few of them have a sufficiently narrow attachment to provide a suitable axis round which to twist. When a loop of intestine undergoes torsion (volvulus) the symptoms will be those of acute intestinal obstruction; such a volvulus may reduce itself spontaneously, so there may be a history of previous similar attacks. The pain of torsion of an organ is like the pain of an inflammatory lesion; thus torsion of the omentum, particularly if it is adherent in the right iliac fossa, may simulate appendicitis. The omentum rarely undergoes torsion unless it is attached at its apex. Ovarian cysts which twist on their pedicles are usually between 5 and 10 cm. in diameter and can often be felt above the pubes; the smooth rounded nature of the swelling presents early in the attack, and the fact that it is more mobile than an appendix abscess will give away the diagnosis.

Torsion of the gall-bladder or of the spleen is so rare that it is unlikely that the diagnosis would be made before operation.

Haemorrhage

Spontaneous intraperitoneal haemorrhage of sufficient degree to cause severe blood loss is very rare except in cases of ruptured ectopic gestation; the sudden onset, tenderness, and perhaps the presence of a swelling felt on vaginal examination, together with the menstrual history, will usually make the diagnosis clear, often before there is evidence of blood loss. Of greater difficulty in diagnosis is the bleeding into the peritoneum which may be associated with the rupture of a Graafian follicle. The blood loss is not severe, but it is sufficient to irritate the peritoneum and causes low pain, referred to one side or the other; if on the right it is likely to be confused with appendicitis. This condition usually occurs in young women between the ages of 15 and 25 and about the mid-menstrual period; tenderness is most severe immediately above the pubes, and in the pelvic peritoneum when palpated through the rectum. The condition will settle down without operative treatment, but if the diagnosis is in doubt laparotomy should be undertaken.

A dissecting or a leaking aneurysm of the aorta, due to atherosclerosis, may give rise to sudden abdominal pain suggesting an intraperitoneal catastrophe; a difference between the two femoral pulses, or the appearance of bruising, may lead to a correct diagnosis before a laparotomy is performed.

Conclusion

There are many patients who have mild attacks of indigestion, perhaps with intestinal colic and vomiting, for which no cause can be found; these may be due to dietary indiscretions or to the ingestion of some toxic substance. It is most important that such a condition should not be diagnosed in a patient who has an acute abdominal lesion which is likely to lead to peritonitis. In particular, no patient with acute inflammatory disease in the abdomen should be given analgesics or be treated by sulphonamides or the antibiotics until a definite diagnosis has been confidently made and a decision has been reached that the patient does not require an urgent laparotomy. The mortality of acute abdominal emergencies has been greatly reduced in recent years, but the commonest cause of a fatal outcome is still delay in seeking advice or in making a correct diagnosis.

Next article on Emergencies in General Practice.—"The Acute Abdomen in Children," by Mr. Denis Hindmarsh and Professor Donald Court.

PULMONARY CIRCULATION AND RESPIRATORY FUNCTION

SYMPOSIUM AT ST. ANDREWS

[From a Special Correspondent]

The 544-year-old University of St. Andrews gave renewed evidence of its vitality and leadership in medicine by imaginative organization of, and generous hospitality to, a conference of over a hundred visitors who met in Dundee on September 15 and 16 to discuss pulmonary circulation and respiratory function.

Pulmonary Circulation

Professor D. R. Dow, Master of Queen's College, welcomed the guests, and Dr. I. de Burgh Daly, F.R.S., opened the proceedings with a convincing demonstration of the sympathetic vasomotor innervation of the pulmonary blood vessels in the dog. Stimulation of the stellate ganglion caused an 80% increase in pulmonary vascular resistance under carefully controlled conditions. Professor J. McMichael and Dr. J. F. Goodwin later supported this view with evidence from the use of ganglionic blocking drugs in man, while Dr. P. Wood showed that minute doses of acetylcholine could also effect some lowering of the pulmonary artery pressure in cases of pulmonary hypertension.

Dr. G. de J. Lee presented evidence that under normal conditions the lung vessels in man were in fact very passive in their behaviour, playing little part in the reflex responses following a Valsalva experiment. He further demonstrated that the uptake of oxygen in the lungs is rapid just after cardiac systole and very slow in diastole, which suggests gross capillary pulsation of the alveolar capillaries and a very variable speed of flow through them, rapid in systole and slow in diastole. Professor McMichael drew attention to a discrepancy in estimates of the volume of blood normally present in the human lung capillary bed, Roughton's figure being 60 ml., while estimates by other methods put it much higher—perhaps 300 ml. Dr. D. V. Bates held that Roughton's figure was correct, while Dr. Daly thought the question was still open. Dr. P. Hugh-Jones had suggested that Roughton's figure might signify blood undergoing active gas exchange under resting conditions, leaving a considerable capillary reserve for exercise. Dr. K. W. Donald recalled Wearn's observations of phasic opening and closing of alveolar capillaries in the lungs of the cat, but the validity of these observations was questioned. Dr. W. A. Briscoe, however, considered that blood flow through poorly ventilated alveoli must be reduced, and this might be one of the teleological functions of a vasomotor control of the lung vessels. Professor McMichael reminded the audience of the controversy which has arisen concerning the mechanism of constriction of the pulmonary vessels which accompanies asphyxial states in bronchitis and emphysema. It did not seem to be a simple local vascular response to anoxia, as was thought previously.

Expansion of Lungs at Birth

Dr. G. S. Dawes dealt with the switch-over to normal breathing at the birth of lambs. The lungs of the early foetus are difficult to expand, but the resistance to expansion diminishes towards term, though it is still quite considerable. When the ventilation of the lungs is inadequate the ductus arteriosus remains open longer. In some experiments it could be demonstrated that with low oxygen inhalation the ductus opened and with air breathing the ductus contracted. Professor I. Donald presented records from the human infant at the moment of birth showing the immense inspiratory effort (minus 60 cm. water) needed to expand the foetal lungs for the first time; pulmonary expansibility approached the normal only after about six hours of life. He emphasized the high neonatal mortality from defective respiration and demonstrated his ingenious positive pressure machine for treatment of these respiratory difficulties.

Circulation in Mitral Stenosis

Discussion of the lung circulation in mitral stenosis was ably opened by Dr. K. W. Donald. Professor P. R. Allison discussed the value of pressure records from 157 punctures of the left atrium through the left bronchus. No untoward consequences of this procedure had occurred. Dr. Wood mentioned that the transthoracic left atrial puncture more recently recommended in Sweden was too often followed by haemorrhage. Professor Allison found the ratio of left atrial pulse pressure to systolic atrial pressure a better index of mitral incompetence than Wood's method, which measures the rate of fall of pressure in the left atrium during ventricular diastole, but his statement did not pass unchallenged by Dr. Wood. There was general acceptance of the validity of "wedged" pulmonary catheter tracings as reflecting fairly accurately the left atrial pressure curve, though it was agreed that they were less valuable under conditions of low pressure and when the pulmonary arteries were themselves thickened.

Generally the pulmonary capillary pressure did not rise above 30 mm. mercury in mitral stenosis, but Wood emphasized that pressures could on rare occasions rise much higher without frank pulmonary oedema. Among the suggested explanations for this surprising observation were: (1) A "barrier" against leakage from the capillary (Wood). (2) Rapid removal of fluid by lymphatics, or accumulation in the interstitial spaces (Professor W. M. Arnott). (3) There was a "subclinical" stage of transudation (Bates). Professor McMichael said that in spite of high pressures in the vascular bed of the lungs in mitral stenosis their capacity did not seem to be increased. This might be accounted for by the "induration" of the pathologists. Dr. Bates agreed that the lungs were stiff in mitral stenosis and often showed a defect of gaseous diffusion.

Other Factors in Pulmonary Hypertension

Other factors in the development of pulmonary hypertension were discussed. Professor A. A. Liebow (Yale) demonstrated beautifully the enormous anastomotic developments of the bronchial circulation when the pulmonary vessels proper were obstructed. Professor McMichael doubted whether this anastomotic circulation played much immediate part in the production of pulmonary hypertension, arguing that patent ductus could exist for decades without pulmonary hypertension. Dr. Wood said that 38% of 45 large patent ductuses developed pulmonary hypertension, against 57% of 54 ventricular septal defects and 16% of atrial septal defects. Dr. Maurice Campbell thought that many severe pulmonary hypertensions were reversible, especially in early life. Reversal of gradually developing severe pulmonary hypertension of mitral stenosis might be a very slow process.

Dr. W. Whitaker showed the stages of development of muscular walls in the pulmonary arterioles in pulmonary hypertension. Normally, practically no muscle was visible. In severe cases of pulmonary hypertension the changes in the arterioles were like those of malignant hypertension. Professor A. Lendrum showed some beautiful histological preparations suggesting that "fibrinoid" change was in fact a permeation of the vessel wall with fibrin. He produced intriguing evidence, based on a comparison with "sensitization arteritis," that sensitization or hyperergy could play an important part in the production of fibrinoid change. Dr. K. W. Donald showed a section of a pulmonary arteriole in pulmonary hypertension complicating patent ductus, which seemed practically obliterated at its distal end with sinusoid-like branches leading off proximal to the occlusion.

Sir RUSSELL BROCK thought that the infundibulum of the right ventricle, like the bulbus cordis of lower vertebrates, had a separate function and contracted later than the main part of the ventricle. Professor I. HILL had electrocardiographic evidence compatible with this hypothesis. Sir Russell Brock suggested that severe cyanotic attacks in Fallot's tetralogy might result from increased tone in the infundibulum narrowing the entrance to the pulmonary valve and thus reducing pulmonary flow. In this he was supported by Dr. Wood. Professor R. WALMSLEY pointed out, however, that normally the interior surface of the infundibulum was quite smooth and that thick muscular ridges within it must be pathological. Sir Russell Brock demonstrated that after valvotomy in pulmonary stenosis there was often a vastly improved pulmonary blood flow, although right heart pressures might not be very significantly changed from the pre-operative state. The normally low resistance of the lung vascular bed contributed to this.

Measurement of Pulmonary Function

Professor W. MELVILLE ARNOTT reviewed the measurement of pulmonary function under three heads : (1) ventilation, (2) gaseous interchange, and (3) circulatory. Stiffness of the lung could now be measured by a pressure-volume graph traced by an ingeniously devised machine. Dr. C. M. FLETCHER showed simple portable " pocket " devices devised by Dr. B. M. Wright for making measurements of total ventilation and maximum breathing capacity. Professor J. L. D'SILVA was critical of over-simplified spirometry, but HUGH-JONES and Dr. C. B. MCKERROW gave some good evidence of the value of simple quick measurements in practical tests.

Drs. Fletcher and Hugh-Jones recommended the use of a specific measure of pulmonary ventilation on standard exercise as a percentage of maximum breathing capacity as a " dyspnoeic index." They thought this was of special value as a screening test before other more complex and detailed tests of lung function. Drs. Donald and Briscoe had doubts of the value of an index of dyspnoea because of the subjective character of the symptom—" shortness of breath." Dr. Bates discussed the measurement of the diffusing capacity across the alveolar membrane and illustrated its clinical use. Dr. C. M. OGILVIE, however, seemed to think that the range of results in such measurements was still too wide for immediate application to clinical problems and more work was needed.

Professor J. P. DUGUID demonstrated an automatic lung section scanning device for counting alveolar walls and showed how this could be used to estimate the total surface area of the alveoli. Professor J. GOUGH demonstrated the character of pathological changes in whole lung sections —showing, for example, that severe and fatal asthma did not necessarily cause loss of alveolar walls and that there was a considerable local anatomical obstruction to pulmonary arteries in the massive fibrosis of miners. Dr. Fletcher questioned whether purely local changes in the pulmonary vascular bed could really cause pulmonary hypertension. Dr. H. Doss (Cairo) showed that, in spite of widespread anatomical vascular narrowing in the lungs following bilharzial embolism, there was some functional element in this type of pulmonary hypertension, as pulmonary pressure fell considerably on giving hexamethonium without corresponding changes in cardiac output.

An account of the present-day breathing machines for use in cases of respiratory paralysis was given by Dr. L. G. C. PUGH.

Dr. ROBERT COOPE discussed the problem of integrating these spectacular physiological advances into clinical practice. He thought every aspirant to consultant status in a teaching hospital should have a training in these and similar investigative techniques. This would ultimately lead to the improvement of clinical medicine. Other speakers suggested that such research could also be undertaken by good doctors without detriment to their clinical skill.

CHARTERED SOCIETY OF PHYSIOTHERAPY

DIAMOND JUBILEE CONGRESS

The Diamond Jubilee of the Chartered Society of Physiotherapy was celebrated as part of the Society's annual congress in London on September 22 and 23. The Society was formed, as the Society of Trained Masseuses, by a group of women, including Dame Rosalind Paget and Miss Lucy Robinson, who wished, first, to provide facilities for an adequate training in massage, and, secondly, to ensure a code of ethics for those who practised after qualification. In 1900 the Society became incorporated, with a membership of about 250. When its royal charter was granted in 1920 the membership was about 5,000, and now the number of chartered physiotherapists on its verified register is 14,808.

The Minister's Address

The congress was opened by the MINISTER OF HEALTH, Mr. Iain Macleod, who said that in the sixty years of the Society's history there had been enormous developments in physiotherapy, as in all branches of medicine. In this field the pace had quickened greatly over the last few years, especially perhaps the last fifteen years, owing to the impetus given by the urgent and compelling needs of war, in which physiotherapists were able to play a signal part. New methods, new techniques, new forms of apparatus were being studied, but it was even more important to notice how the role of physiotherapy itself had changed in the course of the years until now it played a vital part in the wide and complex field of rehabilitation. When mobility could be given to the handicapped, a fuller life to the disabled, when enjoyment could be given back again to those who suffered, the physiotherapist was conferring benefit not only on the individual patient but on the community itself, and particularly perhaps on the hospital service, which carried such a heavy share of the National Health Service. The annual report of the Ministry of Health for 1954 mentioned the 10% reduction (50,000) in the waiting-lists for hospitals. This was an enormous step forward, but there was still a long way to go, with 450,000 people on the waiting-list. He was quite certain, however, that what had been achieved was in part a reflection of the work of physiotherapists over the years.

Hope of Agreed Legislation

The Minister went on to say that in view of the great advances in this field and the ever-quickening pace, it was natural that the question of standards and qualifications should be ever present in the minds of those who guided the Society. He mentioned the work of the Cope Committee, which had studied the various professions allied to medicine, their scope and the qualifications which they demanded. He was well aware that the Cope Committee report was not received with universal acclamation, and the same was true of the regulations which he himself issued last year as a temporary measure until it was possible to bring forward agreed legislation in these fields. But a working party was set up, and he was grateful for the participation of the representatives of the Chartered Society. There were still many organizations representative of the professions to be consulted, and it was his aim to reach agreement between them all. It remained his intention to introduce permanent legislation to take the place of the temporary regulations which he laid before the House of Commons a year ago.

Sir HAROLD BOLDERO, chairman of council of the Chartered Society, who presided, in thanking the Minister, said that the ministerial eye must necessarily range over an immense field of activities, and physiotherapy must take its due place, but this specialty played a far from negligible part in the National Health Service. The report of the Ministry revealed that the physiotherapists working in the Service gave 22.5 million separate treatments during the year to 1,750,000 patients.

The opening lecture of the congress was given by Professor G. PERKINS on "Progress in the Treatment of Fractures," and the ensuing time was filled with lectures and demonstrations on chronic respiratory diseases, the place of the physiotherapist in cardiac surgery, the application of progressive resistance exercise in physiotherapy, the elderly sick, and other subjects.

MEDICAL DEFENCE UNION

ANNUAL MEETING AND REPORT

For the first time for 27 years the annual general meeting of the Medical Defence Union was held in a provincial city instead of London. The meeting was at Bristol, and was held on September 20 under the chairmanship of Mr. St. J. D. BUXTON, in the unavoidable absence of the president, Dr. S. COCHRANE SHANKS.

The Legal Aid Scheme

Mr. BUXTON delivered the address. After a brief account of the history of the Union—it is 70 years old this month—and of the nature of its work, Mr. Buxton reviewed the recent trends in medical litigation. After the hospitals were taken over by the State in 1948, their local support rapidly disappeared (though it was now reviving), he said, the staff became paid servants of the State, and the former glory surrounding the hospital committee and medical staff had almost gone. These changes, the alteration in the law, and the introduction of the legal aid scheme all appeared factors in the increase of actions brought against doctors and hospitals. The legal aid scheme made it possible for those without adequate means to bring their case before the Courts. The majority were successful. During the last three years between 80 and 90% of legally assisted litigants had won their cases in the Queen's Bench and Chancery Division, and over 50% had been successful in the Court of Appeal. Out of those applying for legal aid—nearly a quarter of a million—rather more than half had been granted it, but in only 60 out of the 150,000 cases (0.04%) was there known to have been criticism from the Bench. The scheme bore harshly, however, on the successful defendant, as he was unable to collect his costs. The Medical Defence Union considered this lack of provision for the successful defendant more than harsh, went on Mr. Buxton, and an official document had been addressed to the Lord Chancellor inviting him to consider an amendment to the existing provisions.

Describing the activities of the M.D.U., Mr. Buxton touched on the qualifications for membership. Besides the recent admission of dental surgeons without medical qualifications and of provisionally registered medical practitioners, the council was keeping under review the needs of overseas members, particularly as the graduates of the new medical schools in the West Indies and Africa were applying for membership.

At the conclusion of the meeting Dr. S. COCHRANE SHANKS was re-elected president for the 1955–6 session and Dr. HENRY ROBINSON treasurer.

Annual Report

The annual report and statement of accounts for 1954–5 records a total membership (on July 15, 1955) of 41,561, of whom over 3,000 joined during the year. The accounts for the year 1954 show an excess of expenditure over income of £139 in a total expenditure of over £87,000. This is a considerable improvement on the previous year, when the deficit approached £5,000. Nearly £58,000 was spent in legal charges, disbursements, and indemnity claims.

Warnings are given on the questions of unregistered anaesthetists and "telling the patient." As a result of several inquiries during the year, doctors are again urged in the report to discountenance the employment of members of the nursing staff as anaesthetists—as apparently happens in some hospitals—and not to associate themselves with such arrangements, except in cases of the gravest emergency where a second practitioner cannot be obtained. Such a course, besides at once raising the issue of "covering," raises also the more serious one of responsibility if an accident should occur. It is often difficult to know how much to tell a patient or his relatives, and what is best medically is not always soundest legally. Practitioners asked by letter for information about the care or treatment of a patient are recommended to take advice from their Defence Union before replying. The report draws attention to the recent case of a medical practitioner, a co-respondent in a divorce suit, who admitted adultery with a patient. The case was considered by the disciplinary committee of the G.M.C., but the doctor's name was not erased from the *Register*. The report points out that, in the Union's view, this decision turned very much on the facts of the particular case: "it should not be assumed that it represents any change of thought on the part of the General Medical Council."

Other subjects discussed in the report include the right of provisionally registered practitioners to accept fees for "private practice" arising from hospital duties (in the opinion of Counsel this is not permissible under the terms of service), the change of Scots Law resulting in boards of management of N.H.S. hospitals being held responsible for negligence of their resident medical staff, statute-barred actions (the time limit is now three years for the institution of proceedings against public authorities or their staffs), and the inability of Fellows of the Royal College of Physicians of London to sue for their fees. With regard to the last, the council of the Union has suggested to the Royal College that the time has now come for its debarring by-law to be varied or cancelled.

VISIT OF RUSSIAN DOCTORS

As already announced in the *Journal* (August 6, p. 369) six eminent members of the Russian medical profession are visiting Britain this month as guests of the British Medical Association. In making the arrangements for their visit, the Association is indebted to the Soviet Relations Committee of the British Council for its valuable co-operation.

Below we summarize the programme of medical visits and official entertainments arranged for the Russian doctors. They will be entertained in London, Edinburgh, Glasgow, Birmingham, Cambridge, and Oxford.

Monday, October 17.—Luncheon with British Medical Association at B.M.A. House; supper with Royal Society of Medicine.

Tuesday, October 18.—Postgraduate Medical School of London; dinner with University of London.

Wednesday, October 19.—Wellcome Foundation; luncheon with Society of Apothecaries.

Thursday, October 20.—National Institute for Medical Research and Imperial Cancer Research Laboratories, Mill Hill; dinner with H.M. Government.

Friday, October 21.—Middlesex Hospital; luncheon with Royal College of Surgeons of England; dinner for ladies with Medical Women's Federation; theatre and supper for remainder of party with College of General Practitioners.

Monday, October 24.—Medical institutions in Edinburgh; luncheon with University of Edinburgh; Department of Health for Scotland; cocktail party with Royal College of Surgeons of Edinburgh; dinner with Royal College of Physicians of Edinburgh.

Tuesday, October 25.—Luncheon with Lord Provost of Glasgow; medical institutions in Glasgow; reception by Royal Faculty of Physicians and Surgeons of Glasgow; dinner with British Medical Association.

Wednesday, October 26.—Medical institutions in Glasgow; luncheon with University of Glasgow; film show at Glasgow Regional Office of the British Medical Association.

Thursday, October 27.—Queen Elizabeth Hospital, Birmingham; reception by Birmingham Division of the British Medical Association.

Friday, October 28.—Neurosurgical Centre, Smethwick; luncheon with Lord Mayor of Birmingham; Birmingham medical school; dinner with Dean of the Medical Faculty of the University of Birmingham.

Sunday, October 30.—Cambridge Division of the British Medical Association, for visits to colleges and dinner; reception by Mayor of Cambridge.

Monday, October 31.—Cambridge medical school; luncheon with Regius Professor of Physic; Papworth Village Settlement; reception by Vice-Chancellor of the University.

Tuesday, November 1.—Luncheon with Oxford Division of the British Medical Association; visits to colleges; dinner with Vice-Chancellor of the University.

Wednesday, November 2.—Oxford medical school; Radcliffe Infirmary.

Thursday, November 3.—Luncheon with Royal College of Physicians of London; evening party at Soviet Embassy.

Friday, November 4.—The visitors will be introduced to the Council of the British Medical Association, which will be in session; British Red Cross Society; farewell dinner with British Medical Association at B.M.A. House.

In addition, a number of excursions and other social entertainments have been arranged.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

LORD NUFFIELD'S GIFT

Lord Nuffield received a great ovation when he rose to make an impromptu speech at the annual dinner of the Royal College of Obstetricians and Gynaecologists, held on September 23 at the Dorchester Hotel. A few minutes before, Sir Arthur Gemmell, the president of the College, had announced that Lord Nuffield had given £75,000 from his own private resources to the fund being raised for the purpose of building, equipping, and maintaining the College's new headquarters in London. A further £50,000 was being donated through the Nuffield Provincial Hospitals Trust. Sir Arthur said that the name of the College's new headquarters would be Royal College of Obstetricians and Gynaecologists, Nuffield College, Regent's Park. Lord Nuffield, in a few brief remarks, said that he had for a long time thought that he should take some interest in obstetrics and gynaecology. "We are now beginning to wake up to the fact that the ladies ought to have a little assistance." In the future everything possible should be done to bring about childbirth in a fit and proper way, and Lord Nuffield hoped that anything he had been able to do would be a help in that direction.

College and Commonwealth

Earlier in the proceedings, Sir Ronald Weeks, proposing the toast to the College, described the progress which had been made in the plans for the College's new building. The site in Regent's Park was secure, and they were at least half-way to the target figure of £400,000. He would be disappointed if the foundation stone was not laid in 1956. Sir Ronald paid a tribute to the hard work of the council of the College and of Sir Arthur Gemmell, who had filled the office of president with the highest distinction. In reply Sir Arthur said that in every sphere the work of the College was going forward and in many spheres it was expanding. The number of candidates sitting for the diploma had doubled. The College had a special importance in the Commonwealth, and fellows and members in South Africa had asked for a regional council to be set up there. With the agreement of Sir Arthur Sims two Sims-Black professors had been appointed for 1956—one to visit Australia and the other South Africa and Rhodesia. The fund for the new building had still some way to go before the target figure was reached, and there had been some recasting of the plans in order to secure the interest of others who were well disposed towards the College. In conclusion Sir Arthur thanked the council of the College for its unfailing support.

Part-time Consultants

The health of the guests was proposed by Mr. V. J. F. Lack, and Mr. A. J. Espley, chairman of the Institute of Obstetrics and Gynaecology, replied. After congratulating the College on electing Mr. Charles Read as its next president, Mr. Espley remarked that he had something to say to the Minister of Health, who was one of the guests at the dinner. Whatever might be done in the future, he sincerely hoped that the services of part-time consultants would be retained, for they made an invaluable contribution to the efficiency of the N.H.S.

Nova et Vetera

MEMORIAL TO JAMES PARKINSON

BICENTENARY OF BIRTH

> And some there be, which have no memorial; who are perished, as though they had never been.
>
> *Ecclesiasticus*, xliv, 9.

Although James Parkinson provided one of the most familiar eponymic terms in medicine, little biographical information about him was available until the publication earlier this year of a memoir by Dr. A. D. Morris.[1] This coincided with the bicentenary of Parkinson's birth on April 11, 1755. Dr. Morris showed Parkinson as a most versatile character. He was born in Hoxton, London, the son of a surgeon, and he lived there all his life. The site of his house, No. 1 Hoxton Square, is now occupied by a factory.

In 1817 he published his *Essay on the Shaking Palsy*. This classical description of the disease which now bears his name earned him the honorary gold medal of the Royal College of Surgeons in 1822.

Dedication of Memorial at Shoreditch

In addition to a busy practice and the pursuit of his scientific and political interests, Parkinson devoted much time to the interests of St. Leonard's Church, Shoreditch, where he had been baptized and married, and where he was buried in 1824. His tombstone has long disappeared, no portrait of him is known, and there was no memorial to him. This last omission has now been rectified, principally through the efforts of Dr. Morris. On September 17 a memorial tablet was unveiled and dedicated at St. Leonard's Church. It was the gift of members of the nursing staff of St. Leonard's Hospital, which stands on the site of the parish infirmary to which Parkinson was visiting physician. The vicar, the Rev. Meredith Davies, conducted the service

[1] *Lancet*, 1955, **1**, 761.

[2] *James Parkinson, 1755–1824. A Bicentenary Volume of Papers dealing with Parkinson's Disease.* Edited by Macdonald Critchley; in collaboration with Sir Francis Walshe, W. H. McMenemey, and J. G. Greenfield. London: Macmillan and Co.

and gave the address. He said that although Parkinson's name was perpetuated in our language the man himself had been forgotten. Dr. Morris had brought to light Parkinson as he really was and had interested local people sufficiently for them to subscribe to a memorial. Besides being a physician Parkinson was a geologist and a political and social reformer. He was a marginal scribbler who almost re-wrote the books he read. An enthusiastic seeker after truth he eagerly shared new discoveries and interpreted them in terms which the plain man could understand. His later years were more and more concerned to drive home one truth—that human personality was more important than any system.

Place of Pilgrimage

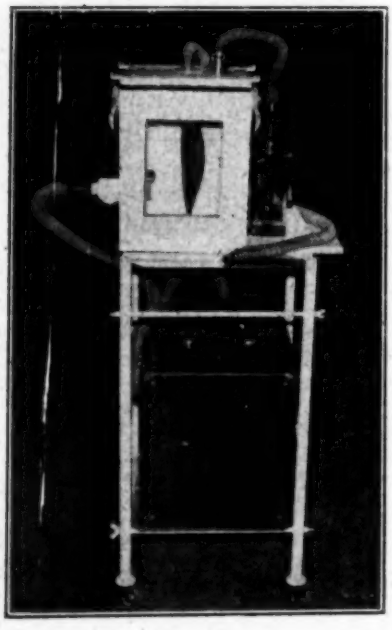
Dr. Morris, a former medical superintendent of St. Leonard's Hospital, unveiled the memorial tablet, an act which, he said, meant the realization of a long-cherished hope that one day James Parkinson would be commemorated in his own church. He referred to Parkinson as a man with a capacity for hard work and an ability to find time for everything, shy and retiring, combining meekness of spirit with firmness of determination. Dr. Morris expressed the hope that St. Leonard's Church would in the years to come be a place of pilgrimage for the nurses and others connected with St. Leonard's Hospital.

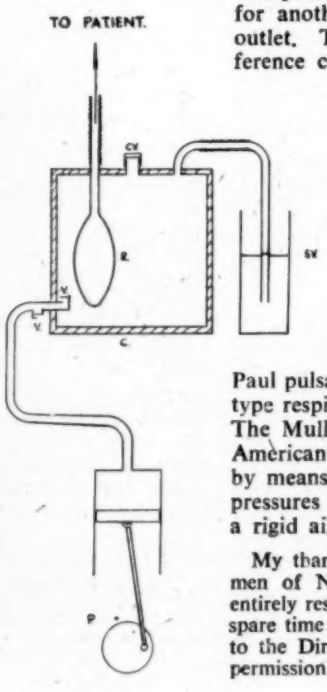
A symposium on Parkinson's disease, including a biographical study and a reproduction of the text of the *Essay on the Shaking Palsy*, is to be published this month.[2]

Preparations and Appliances

A SIMPLE MECHANICAL DEVICE FOR INFLATION OF THE LUNGS

Dr. A. S. Gardiner, of the General Hospital, Taiping, Malaya, writes: In these days of controlled respiration the anaesthetist who has to work without trained assistants may find himself hard pressed to perform all the duties expected of him. In these circumstances a mechanical pulmonary inflator relieves him of much anxiety. I describe below an attachment to the pump of the Mullikin automatic respirator which serves this purpose. It is simple to construct and cheap, and no doubt similar models could be made for attachment to a wide variety of "iron lung" pumps which are often found in out-of-the-way places.





The attachment consists of a suitable-sized airtight chamber (C) containing a rubber reservoir bag (R) which is part of the anaesthetic circuit. The pressure phase of the pump (P) is used to compress this bag, and its vacuum phase is eliminated by a gravity-type valve (V): during this phase air escapes from the control valve (CV) and the pressure in the chamber rapidly falls to atmospheric, allowing re-expansion of the reservoir bag. The maximum pressure obtainable is 20 cm. of water, and in practice it has been found that a rapid rise and fall occurs, while the pressure remains atmospheric for three-fifths of the cycle. A safety-valve (SV) is incorporated which can be pre-set to any desired level to release any excessive pressure; and the lid of the chamber can be quickly opened to provide easy access to the reservoir bag for manual compression should the pump fail (or the electricity supply be cut off). Some technical details of the construction follow.

1. The chamber is made of wood $\frac{5}{8}$ in. (1.6 cm.) thick and lined with zinc. Its internal dimensions are 30 by 30 cm., and its height was calculated from the formula

$$H\ (\text{cm.}) = \frac{\dfrac{P_1\ (V_1+V_2)}{P_x} - V_2}{A}$$

where V_2 = volume of tube connecting pump to attachment (c.cm.), P_x = maximum pressure required (cm. water), A = cross-sectional area of attachment (=900 square cm.), and V_1 is the known volume of an airtight vessel which was attached to the pump to determine the rise of pressure produced; this pressure was measured = P_1 (cm. water). One side has a plate-glass window 25 by 30 cm.; the lid is lined with "sorbo" rubber, and its hinges are elongated to allow for compression by the four toggle clamps.

2. The unidirectional valve consists of a component outside, and one inside, the chamber. Each has a disk made from Tufnol sheet covering an opening in the inlet pipe, and retained in place by a screwed-on brass ring.

3. The control valve is simply an adjustable air exit port. It consists of two brass collars closed in at the top. The inner one is fixed and communicates with the chamber; it is cut away completely for one-third of its circumference, and partly (in the form of two narrow horizontal grooves) for another one-third, to facilitate fine adjustment of the outlet. The outer collar also has one-third of its circumference cut away, and by rotating it the size of the port can be varied from closed to fully open, with any intermediate position.

4. The safety-valve is a water-depression type: a wide-bore glass tube dips into water contained in a large glass jar. The central tube can be racked up or down, and is graduated in centimetres.

5. The pump.—Owing to the size of the chamber and the wastefulness of the control valve, the pump must supply a relatively large volume of air. For this reason, pumps with a small stroke-volume—for example, the Bragg–Paul pulsator—are unsuitable, while those in use with cabinet-type respirators (such as the Drinker) would be satisfactory. The Mullikin mechanical respirator pump used here is an American machine producing negative and positive pressures by means of bellows actuated by an electric motor; these pressures are normally conducted along a flexible pipe to a rigid airtight shield worn around the patient's chest.

My thanks are due to Staff-Sergeant A. V. Coleman and his men of No. 1 Station Workshop, R.E.M.E., who have been entirely responsible for the construction of this apparatus in their spare time; and to their commanding officer. I am also grateful to the Director of Medical Services, Federation of Malaya, for permission to publish.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Uterine Ischaemia and Pre-eclampsia

SIR,—We are somewhat perturbed by the pessimistic tone of the leading article on "Uterine Ischaemia and Pre-eclampsia" (*Journal*, September 10, p. 664), and particularly by your summary dismissal of the possible usefulness of studies on analogous syndromes in animals in increasing our understanding of human eclampsia.

The experimental production in a suitable animal of a disease analogous to that in the human being has on numerous occasions been the starting-point for conspicuous advances in knowledge of the human disease. We believe that this may well be the position now in regard to human eclampsia and the syndrome of toxaemia of pregnancy in sheep. Although there are obvious differences between the diseases in the two species we cannot agree with your view that "toxaemia of pregnancy in animals differs fundamentally from the human type." The signs of some vitamin deficiencies vary greatly from one species to another, but no one would now argue that they are not the consequences of the same disorder. A comparison of the pathological physiology of toxaemia in man and sheep shows agreement in a surprisingly large number of particulars.

In sheep, as in man, the disease occurs chiefly during the last third of pregnancy; it is much more common in twin pregnancy and in pregnancy complicated by hydramnios (hydatidiform mole is unknown in sheep); the disease may manifest itself in a form without fits comparable to pre-eclampsia and in a form with fits comparable to eclampsia. In rare cases a fulminating post-partum form with fits occurs; the disease in its less severe forms almost certainly ceases if pregnancy is terminated, when the animal makes an uneventful recovery; the death of the foetus occurs if toxaemia is severe and prolonged, but the mother may die without prior death of the foetuses.[1] Sheep which are allowed to make high weight during early pregnancy are much more prone to develop toxaemia during the last third of pregnancy and the attack rate of the disease can be reduced most effectively by suitable antenatal care designed to prevent excessive weight in early pregnancy[2] as in the human disease[3,4]; while the pattern of the renal dysfunction with reductions in the glomerular filtration rate, renal blood flow, and filtration fraction, which are unaccompanied by morphological change and probably completely reversible,[5] is very similar to that reported in recent studies of human toxaemia,[6–8] although the massive proteinuria seen in man is rarely, if ever, observed in sheep.

The main point of dissimilarity between the two diseases is the absence of hypertension in the sheep.[9] Although hypertension is nearly always present in human eclampsia and is indeed usually considered to be one of the diagnostic triad of signs, eclampsia can occur in normotensive women, and hypertension may yet prove to be a secondary manifestation, commonly accompanying the eclamptic process, but not essential for its primary development. Oedema of the limbs is also less pronounced in ewes than in women, almost certainly due to differences in anatomical structure, for oedema of the limbs is a very rare condition in sheep. The livers of affected sheep contain much fat, as do those of affected women, but the centrilobular haemorrhages seen in the human disease are absent. Placental lesions are not seen in the sheep disease; they are commonly present in human eclampsia, but their presence is variable and is not now considered to be an essential feature.

While more comprehensive studies of the toxaemic syndrome in general may reveal greater differences between the disease in man and in the sheep, we consider that at the present time the similarities between the two diseases far outweigh the differences. As we are now able to induce toxaemia of pregnancy experimentally in a high percentage of sheep,[9] it seems well worth while to use this experimental disease as a model for the study of the metabolic toxaemias of late pregnancy, in the hope that such studies will throw some light on the human disease as well as contributing to the control and prevention of the natural disease in sheep.—We are, etc.,

G. S. DAWES.
H. B. PARRY.

Oxford.

REFERENCES

1 Parry, H. B., *Toxaemias of Pregnancy: Human and Veterinary* (Ciba Foundation Symposium), 1950, p. 85. London.
2 —— *Proc. Brit. Soc. Anim. Prod.*, 1955, in press.
3 Hamlin, R. H. J., *Lancet*, 1952, **1**, 64.
4 —— *Proc. roy. Soc. Med.*, 1953, **46**, 393.
5 Parry, H. B., and Taylor, W. H., *J. Physiol.*, 1955, **127**, 54P, and in press.
6 Kenney, R. A., Lawrence, R. F., and Miller, D. H., *J. Obstet. Gynaec. Brit. Emp.*, 1950, **57**, 17 and 960.
7 Assali, N. S., *Ciba clin. Symp.*, 1954, **6**, 3.
8 Govan, A. D. T., *J. Path. Bact.*, 1954, **67**, 311.
9 Parry, H. B., *J. Physiol.*, 1954, **126**, 40P.

Adult Education for the G.P.

SIR,—Dr. R. D. Lawrence (*Journal*, September 10, p. 681) draws attention to a need. Courses of education on a single theme or closely related subjects are wanted by general practitioners. More are needed, and perhaps also more adjustment of those that exist to the family doctor's problems, though there will always be a continued demand for the survey type of course on unconnected subjects.

I am very conscious myself that the rival stimuli of two excellent lectures in a single afternoon, first on chronic chest diseases and then on peptic ulcer, were obliterated in the following week by an admirable demonstration of laboratory technique, followed an hour later by a variety of unusual cases in an out-patient department.

Educational courses round a single subject or theme have two further advantages. It is easier to stimulate and guide the all too latent reading habits of the postgraduate student by limitation to one field, however large. Surely no educational course fulfils its functions unless an increase in reading follows. It is, too, possible in a specialized course to acquire or reacquire skills and techniques in diagnosis and treatment. Nothing is more depressing than the fixity of habit in techniques that develops over years of hard-pressed practice, and nothing more refreshing (in addition to value in practice) than the introduction of new ones.

Lastly, such specialized courses need not be intensive. One day or a half-day a week for two to three months usually suit the general-practitioner student better, and could probably be arranged without undue difficulty by the hospital department concerned.—I am, etc.,

ANNIS GILLIE.

London, W.2.

Intersexuality

SIR,—The articles by Dr. C. N. Armstrong (*Journal*, May 14, p. 1173) and by Dr. G. I. M. Swyer (*Journal*, September 17, p. 709) form handsome contributions to the finer points of sex determination, and are illustrative of the high standard of work performed by the younger school of endocrinologists.

Dr. Swyer quotes two male pseudohermaphrodites, young women of feminine habitus with primary amenorrhoea, one with an enlarged clitoris and the other gave oestrogen withdrawal bleeding. In both cases the chromosomal determination was male by Barr's skin biopsy and the interesting and more recent polymorphonuclear technique of Davidson and Robertson Smith.[1] In the establishment of this new syndrome it is a pity that the argument was not clinched by biopsy of the ovary. The criterion of the female "*propter ovarium mulier est quod est*," of Roman law is the basic principle, and it is of importance to the young girl that ovarian abnormalities should be established with a view to future therapy. In *The Adrenal Cortex and Intersexuality*[2] several of these intersex conditions are illustrated and clinically described with the pathological findings of their gonads. In our series laparotomy has produced its surprises.

Case 34, a true hermaphrodite with ovotestes, was certified as a girl, at 3 registered as a boy, and investigated at the age of 9 in 1936. His build and general behaviour were those of a boy and his penile hypospadias was converted into a urethra. He has proved a useful citizen and is married as a male. Recent examination of his skin by Professor Barr showed the female speck of chromatin. This was at variance with the true sex and is the only wrong answer we have received from him.—I am, etc.,

London, W.1. L. R. BROSTER.

REFERENCES

[1] Davidson, W. M., and Smith, D. R., *British Medical Journal*, 1954, 2, 6.
[2] Broster, L. R., *et al.*, *The Adrenal Cortex and Intersexuality*, 1938. Chapman and Hall, London.

A Simple Blood-grouping Method

SIR,—Mr. J. T. Rice-Edwards (*Journal*, September 10, p. 681) refers to the blood-grouping methods in use in Copenhagen. We have obtained from the Nordisk Insulinlaboratorium a supply of these cards and are testing them in our laboratory at the Leeds Hospital for Women. When we have investigated a sufficient number of cases, we intend to publish the results and a description of the method.—I am, etc.,

Leeds. A. AMBERY SMITH.

Combined Immunization

SIR,—The leading article (*Journal*, September 10, p. 663), coupled with the three most interesting articles by Dr. H. J. Parish, Miss Mollie Barr *et al.*, and Dr. Violet Spiller *et al.* (pp. 631, 635, and 639), must have left many of your readers firmly convinced of the value of the combined prophylactics. The essential point, however, which was brought out by these articles was that (when using separate antigens of the best type) the timetable of immunization recommended by the Ministry of Health—that is, smallpox vaccination at 3 months, pertussis at 4, 5, and 6 months, and diphtheria at 8 months—still remains unquestionably the most effective in so far as antibody responses are concerned. Earlier inoculation than 6 months has been shown in the case of diphtheria to carry a risk of less adequate immunological response and later inoculations in the case of whooping-cough would be a retrograde step, since, to take one year at random, in 1953, of the 243 deaths from this disease, 167 occurred in infants under the age of 1 year.

Many authors have emphasized the value of a combined immunization, since a course of three inoculations is more likely to be completed than five, but if it is now suggested that a further booster dose is to be given at 1 year of age to the children who have received the combined method of prophylaxis then a great part of this advantage has disappeared, since the comparison is now between four and five, coupled with the difficulty of ensuring that mothers do attend with their infants at the correct time for the booster.

While it is true that, with a combined vaccine, very satisfactory Schick conversion rates can be obtained, yet due regard must be paid to the waning of antibody levels with time, for many surveys have shown that immunized children can succumb to the disease—for example, in the county of Staffordshire between 1949 and 1954, of the 302 known cases of diphtheria in children, no less than 73 had records of a previous course of diphtheria immunization. In 20 cases the children were under the age of 5, so that the immunization must have been carried out within the previous few years. Other authorities have quoted similar figures—for example, J. T. George.[1] If immunization is not to fall into disrepute the antigens producing the highest antibody levels should be used.

It was clearly brought out in Barr's article the severe risk of local reactions with combined adsorbed prophylactics—that is, 17 sterile abscesses following 198 injections—and, while the paper records no abscesses following the use of fluid toxoids, yet I have seen such reactions in practice.

The adsorbed antigen is now notorious for its association with poliomyelitis. If the suggestion that the fluid toxoid has now overcome this difficulty is confirmed, this would indeed be a great advance, but there is a sad lack of statistical evidence as to the safety of the new antigen so that reports from authorities who have carried out extensive campaigns would be of great value, and it is to be hoped that some lead may be coming from the M.R.C. shortly.

The addition of tetanus to form a triple antigen is, on the face of it, a simple and satisfactory procedure, but, since adequate protection requires circulating antibody and therefore annual booster doses, it is very doubtful as to whether the present schemes will, in fact, produce any significant effect in reducing the number of cases and deaths. The prospect of 50 million injections annually being required to prevent 70 deaths makes one wonder whether passive immunization is not a more satisfactory alternative for those at risk.

A preservable record card of immunization as you suggest is, of course, a most essential provision for any scheme of mass prophylaxis, and many local authorities do, in fact, furnish the mother with some permanent evidence as to the type of antigen which has been administered. It may be that, in time, a much fuller record booklet of the type seen in France will become universal and be carried almost as a second identity card from birth throughout life.—I am, etc.,

Stafford. HARRY BINYSH.

REFERENCE

[1] Lycett, C. D L., and George, J. T. A., *British Medical Journal*, 1953, 1, 694.

The Whitfield Tradition of Therapy

SIR,—Dr. G. B. Matthews in a kind letter (*Journal*, September 17, p. 737) starts one hare and stirs up a wasps' nest—but then he comes from the country. I would not dare to reply for the psychological wasps, since I have a healthy respect for their stings. The hare is less of a problem: What is Whitfield's ointment? In the last edition of his handbook on skin diseases, Whitfield[1] gave the formula thus:

Benzoic acid	25 grains (1.65 g.)
Salicylic acid	15 grains (1 g.)
Soft paraffin	2 drachms (7.8 g.)
Coconut oil .. .. to	1 ounce (31 g.)

Thus it continued in the King's College Hospital pharmacopoeia. Dermatologists, like composers, enjoy concocting variations on a theme and the variations can be attractive; but there is much to be said for ending with a broad and simple statement of the original theme.—I am, etc.,

London, W.1. DAVID WILLIAMS.

REFERENCE

[1] Whitfield, A., *A Handbook of Skin Diseases and Their Treatment*, 1921, 2nd ed. Arnold.

Position for Delivery

SIR,—While agreeing with Dr. W. N. Leak (*Journal*, September 17, p. 735) that exaggerated lithotomy is theoretically and practically the wrong position for a normal delivery, I must differ from his opinion that the left lateral is better than the dorsal.

He does not state whether his patients have had adequate preparation for labour which enables them to be co-operative and controlled. Those who receive pre-natal instruction are taught to adopt the delivery position—lying on the back supported by pillows at an angle of 30°–45° to the horizontal. It allows easy movement of the knees to the most comfortable and advantageous position during the changing phases and sensations of the second state. Women and perineums do not conform to a rule of thumb, but this position ensures effective control of breathing and expulsive effort and presents to the foetal head the maximum outlet of the pelvis and birth canal. More important, it enables a woman to see and to hear her attendant. Between contractions her legs resume a relaxed and restful position until the head is crowning, when they may be supported, not in stirrups, but at an angle giving the greatest ease of delivery. It enables her to collaborate with her attendant, and when confidence and self-control are maintained, as they are in the large majority of prepared women confined by understanding obstetricians and attendants, the emotional support she requires may be given by word, facial expression, and humane gentleness of approach which she can see and appreciate. The incidence of tears and episiotomies is recorded by many observers to be lower than the accepted average, while strains and hyperextensions do not occur.

In the first stage of labour the woman lies, during contractions, in the left, right, or dorsal position of relaxation, whichever she prefers. Schools in this country are amongst the few who teach the left lateral position for delivery. Most European countries and, almost without exception, the coloured races assume the dorsal or semi-squatting attitude with variations in the position of the legs. This is the outcome of trial and error for generations past by peoples skilled and experienced in childbirth without association with modern scientific concepts. Their results in normal labour are excellent.

Ideally, a woman should be allowed complete freedom of speech and movement during labour. Her psychological rectitude and physical efficiency are enhanced by this precaution. If she is not prepared or, for one reason or another, her behaviour is uncontrolled, analgesia or anaesthesia should be employed, not stern physical and mental restraint. Her wishes must be considered, for "humanity can co-exist with the science of modern obstetrics."[1] Fully conscious women, even to-day, are subjected to the indignity of lithotomy, their hands pinioned to the body or strapped to the bed, robbed of volition or the opportunity of co-operation. The most advantageous position for each individual woman can be obtained by her co-operation with her attendants, and this is only possible when patient and obstetrician have a clear understanding of the psychological and physical phenomena of labour as they concern, in their different ways, the parturient and the practitioner.—I am, etc.,

Petersfield, Hants. GRANTLY DICK READ.

REFERENCE

[1] Mack, Harold C., *Amer. J. Obstet. Gynec.*, 1955, **69**, 933.

Numbering of Fingers

SIR,—The Council of the Medical Defence Union at its last meeting gave careful consideration to a problem that arises from time to time in threatened or actual medical litigation. This problem has been created by the current nomenclature employed by anatomists and surgeons for the designation of the fingers. To do as many do—namely, to number the fingers 1, 2, 3, etc., and to record in the clinical notes, for example, that finger number 3 requires amputation—is to set the stage for a serious surgical mishap. Now and again the surgeon, reading the notes of the case at a later date, before proceeding to operate has counted wrongly by choosing to regard the thumb as number 1 instead of the index finger. In this way the wrong finger has been amputated or chosen for some other operation.

It seems to the Council of the Union that this serious mistake would be obviated if hospital medical officers when writing up clinical notes described the actual finger affected by adopting the designations of "the thumb," "the index finger," "the middle finger," "the ring finger," and "the little finger." It is no part of the duty of the Council of the Union to instruct medical students and others how clinical notes should be prepared, but on this occasion it felt that it would be rendering a real service to its members and to the profession at large if it brought to their notice an obvious and simple way of avoiding an unfortunate mistake that may be followed by medical litigation.—I am, etc.,

ROBERT FORBES,
Secretary,
The Medical Defence Union.

London, W.C.1.

Aortic Stenosis

SIR,—In their article on aortic stenosis (*Journal*, September 24, p. 759) Drs. M. B. Matthews, W. E. Medd, and R. Gorlin state: "It should not be necessary to submit the patient to thoracotomy to demonstrate the severity of the aortic stenosis by measurement of the systolic pressure differential across the aortic valve, as suggested by Brock (unpublished observation delivered to Cardiac Society meeting on April 9, 1954)." To one who is sensitive to the proper principles that should guide medical and surgical practice this statement comes close to professional libel. Before alleging that I made such an outrageous suggestion I think the authors would have been wiser to have asked me whether in fact their memory and impression were correct that I said this at a private society meeting. I presume they would have verified a printed article.

Actually I said nothing of the sort. I pointed out that the presence of an aortic thrill and systolic murmur did not necessarily indicate the presence of significant aortic valve obstruction. In support of this I instanced two cases in which in the course of operation—for example, for an associated coarctation—I demonstrated that there was no pressure gradient across the aortic valve although a firm clinical diagnosis of aortic stenosis had previously been made. I also stated that to publish results of the operative treatment of aortic stenosis without reporting the pressure gradients across the valve was unsatisfactory in that one had an incomplete guide to the presence or severity of the condition. I fully realize that pressure gradients across a valve stenosis are not entirely informative or complete, but they do furnish some information to help us in understanding more about this difficult disease. That is quite a different matter from advocating submitting a patient to thoracotomy to see if he has aortic stenosis severe enough to need treatment.—I am, etc.,

London, S.E.1. RUSSELL BROCK.

Two Cases of Knotted Cord

SIR,—The following two obstetrical cases occurred long ago in my practice and may be of interest to readers.

The first was that of a multipara. It was the patient's third pregnancy, and at full term the foetus was in the occipito-posterior position. This persisted in labour, and internal rotation and forceps delivered a vigorous 9½ lb. (4.3 kg.) baby without mishap. While waiting for the cord to cease pulsation, I observed a knot in the cord, and also the marvellous provision made for the child's safety—namely, two flanges, one above and one below the crucial loop of the knot. I separated this out, and found as I had guessed that it was impossible to lock the knot. One could pull on each end of the cord simultaneously, but no degree of pulling was sufficient to cause locking, and thereby cutting off the circulation. The cord would have ruptured completely from tension if that had been sufficiently exerted, but in no circumstances whatever could the knot be locked. I took immediate measures to preserve and have photographs made of the section of the cord containing the knot.

The first photograph shows the knot as it was at delivery, except that the upper flange originally lay close to the uppermost loop of the knot. The second shows the knot undone to exhibit the flanges freely.

Among those to whom I showed my photographs that evening was a surgical friend in Glasgow Western Infirmary, who I knew would be interested. He was greatly intrigued, and as I was going away he called out in prophecy: "You will get another case of locked cord soon: look out for it." Two and a half weeks later another patient, ten weeks pregnant, entered my surgery to report what was obviously a threatened abortion. Next morning when I called I found in a vessel a complete abortion with membranes unruptured.

I slit the membranes open and found a dead foetus with a tightly locked knot in the cord. So the prophecy came true.

In the Hunterian Museum of Glasgow there is a classical preserved specimen, one of Professor William Hunter's own cases, of a foetus at full term lying in the brim of the pelvis, the anterior wall of the uterus being removed to show a locked knot on the cord running across the child's back. It tells its own pitiful and tragic story. I have reason to believe my case is unique, inasmuch as the child lived by virtue of the special provision made for it, which was not less than providential.

All this took place long ago, before the present regulations, Midwives Acts, etc., were instituted, when it was possible for a general practitioner, sufficiently keen and capable, to do quite distinguished and even original work in the obstetrical field. I cannot imagine a better basis for making and building up a good family practice than highly skilled midwifery.—I am, etc.,

St. Andrews, Fife. JAMES McFARLANE.

Premenstrual Varicose Veins

SIR,—Dr. Stanley Rivlin (*Journal*, September 3, p. 618) points out the exacerbation that occurs in the signs and symptoms of varicose veins in the premenstrual phase. He valuably points out that if the patient is not examined at this time there may be no evidence of the cause. He attributes the condition to the increased venous return from the uterus which dams back the return from the external iliac vein.

This explanation is attacked by Mr. W. G. Mills and Dr. J. S. Norell (*Journal*, September 17, p. 736), who are quite satisfied that the condition is due to the relaxing effect of progesterone on the muscle in the vein wall. Few would dispute that progestin does affect muscle tone all over the body, but have not obstetricians generally been far too ready to accept this explanation for all such effects ever since the physiology of progestin became known? There is a great increase in the venous pressure in the legs in pregnancy; is this what one would expect if we were merely dealing with diminished tone in the wall? Furthermore, according to McLennan,[1] the pressure in the basilic vein is not increased in pregnancy. Surely, in view of this, it is very tempting to accept the damming effect of the increased return in the internal iliac as being at least partly responsible.

Mr. Mills states that if the mechanical explanation is correct, then every woman toward the end of pregnancy would have severe varicose veins. Might I counter that if progestin alone is responsible the result should be the same, because progestin goes on being produced in enormous quantities until the end of pregnancy? Finally, I would point out that I have recently performed two hysterectomies for large uterine tumours, and both have had operative treatment for varicose veins. I do not know what are the relative chances of developing varicose veins from the uterus enlarged by pregnancy and the uterus enlarged by a new growth. Until I know the answer to this question I prefer to think that premenstrual varices are partly due to the effect of progestin and partly due to the obstruction of the increased venous return from the uterus.—I am, etc.,

London, N.W.1. E. ROBERT REES.

REFERENCE

[1] McLennan, C. E., *Amer. J. Obstet. Gynec.*, 1943, **45**, 568.

Ruptured Infected Urachal Cyst

SIR,—I was interested to read Mr. Raymond Helsby's account of a case of ruptured infected urachal cyst (*Journal*, September 3, p. 603). It prompts me to write about a similar case I saw in 1951.

A boy of 19, a labourer, complained of lower abdominal pain for three weeks. The pain was steady and of an aching nature. It felt worse when he stood up straight. During the same period of time he had noted urinary frequency, but he had no urgency, dysuria, or haematuria. He had no abnormal small or large bowel symptoms; his appetite was good and his weight steady. Ten days before admission he noted some blood-stained discharge from his umbilicus. Examination revealed a pale-faced youth, with a hard, non-tender, fixed mass in the mid-lower abdomen. It was pear shaped and extended up to the umbilicus. The latter was slightly reddened and encrusted with old sanguineous discharge. Rectal examination confirmed that the mass extended into the pelvis. His temperature was not elevated (98° F.—36.7° C.) White cell count 10,950 c.mm. with a normal differential. His E.S.R., however, was raised (40 ml. in 1 hour—Westergren). *X*-ray of the lower abdomen showed no abnormal calcification. Examination under anaesthesia suggested that he had a neoplasm, probably arising from a urachal remnant. Cystoscopy revealed some bullous oedema just above the trigone. At laparotomy the mass was found to involve the abdominal wall and the bladder, and several fleshy glands extended to the right iliac vessels. Total removal was clearly quite impossible. A biopsy was taken from the main mass, and the abdomen closed.

The histological findings came as a surprise. Section of the tissue revealed fibrous tissue only, infiltrated with acute and chronic inflammatory cells. There was nothing to suggest any specific inflammatory condition, and there was no evidence of any malignancy.

Some three weeks later the mass was noted to be less hard to touch, and a definite abscess began to point in the lower abdomen to the right of the midline. This was incised and drained, and from the pus released *Actinomyces israeli* was isolated. He was given a six-week course of chloramphenicol with excellent results. The mass rapidly disappeared and both abdominal wounds healed soundly. When seen two months later no trace of any abdominal lump could be found. One year after operation he had gained 40 lb. (18.2 kg.) in weight and his E.S.R. was normal.

There are four main points of interest here: (1) There was little to suggest we were dealing with an inflammatory process in the early stages. His white cell count was within normal limits and he was apyrexial. (2) In his case an organism was isolated, but only after two weeks' anaerobic culture. The finding of *Actinomyces israeli* is indeed a rarity. (3) The absolutely dramatic response to chloramphenicol. This drug was used in a rather experimental manner then, and it is unlikely that we would use it in such a way nowadays. (4) The total disappearance of the mass is in accordance with Mr. Helsby's contention that simple drainage of infected urachal cysts is all that is required in the first instance.

I am grateful to Mr. J. Scholefield for permission to report this case.—I am, etc.,

Winchester. F. T. CROSSLING.

Mitral Valvotomy

SIR,—The article by Dr. J. F. Goodwin and his colleagues (*Journal*, September 3, p. 573) and your leading article (p. 607) provide much help and information in the very topical problems of mitral stenosis and its surgical treatment. I should like, with due deference, to discuss one aspect of the radiological diagnosis of pulmonary hypertension which, when present in mitral stenosis, is a strong indication for surgical interference.

Using radiological criteria which they have previously described,[1] Goodwin and his colleagues have been able to grade almost all of their patients as having O, I, or II degrees of pulmonary hypertension. Personally, I have considerable difficulty in assessing the pulmonary vascular pattern in the radiographs of mitral stenotics, so have many radiological colleagues, and Lodge states[2] "the changes are not sufficiently reliable or constant." Goodwin *et al.* agree that with gross cardiac enlargement or with pulmonary haemosiderosis assessment of the pulmonary arteries for the radiological diagnosis of pulmonary hypertension becomes impossible.

Short horizontal lines seen in the costophrenic angles of chest radiographs—variously called B lines, Kerley lines, but better designated septal lymphatic lines—only occur (in mitral stenosis) in the presence of a pulmonary capillary pressure of over 25 mm. Hg (normal approximately 10 mm. Hg). Goodwin *et al.* make scant reference to their value and significance (other than that they occur in pulmonary hypertension) and the editorial comment does not even mention them.

In a recent paper,[3] we have investigated the nature of these lines and their prognostic significance in mitral stenosis. When the pulmonary capillary pressure exceeds the effective plasma osmotic pressure (20–25 mm. Hg) excessive oedema fluid leaves the capillaries and enters the interstitial tissues of the lung,

some being drained away by the pulmonary lymphatics, which become distended. The B or septal lymphatic lines are the radiological manifestation of this lymphatic distension and interstitial oedema in the peripheral interlobular pulmonary septa. Thickening of the alveolar basement membrane probably prevents the easy passage of the oedema fluid into the alveoli[4 5] and interstitial pulmonary oedema is often found unaccompanied by intra-alveolar oedema.[6] Hayward and Knott[7] have demonstrated by oesophageal pressure recordings that the rigidity of the lung is often much increased and its distensibility reduced in mitral stenosis. They attribute this to interstitial pulmonary oedema and not to passive vascular congestion : this increased lung rigidity is a considerable factor in producing cardiac dyspnoea. There is often a reduction in lung rigidity following successful valvotomy.

If, then, we can diagnose interstitial pulmonary oedema in mitral stenosis, we can select those mitral stenotics who have pulmonary hypertension and whose dyspnoea is caused by pulmonary changes secondary to organic and mechanical mitral valvular obstruction (Goodwin *et al.*). These are the patients that benefit most by valvotomy. Whilst it is admitted that these septal lymphatic lines are radiologically demonstrable in only a proportion of patients with pulmonary hypertension (in our series 30 cases out of 51 with a pulmonary artery diastolic pressure above 25 mm. Hg), it is nevertheless thought that this is the simplest way of diagnosing interstitial pulmonary oedema. Their presence is a strong indication for valvotomy (provided that the clinical and other assessment is satisfactory), and in our series 29 out of the 30 patients made much post-operative improvement. Their absence is, however, by no means a contraindication for valvotomy. It is believed that the identification of these septal lymphatic lines have a definite place in the selection of patients suitable for valvotomy, particularly in those fairly numerous cases where the radiologist or clinician finds the radiological changes in the pulmonary arteries to be equivocal or difficult to assess.

In conclusion, I should like to acknowledge the very considerable value of this, the most recent, and the several previous articles published by the Hammersmith Postgraduate Hospital workers. They have contributed much to the more complete understanding of pulmonary hypertension and of mitral valve disease.—I am, etc.,

London, S.E.1. RONALD G. GRAINGER.

REFERENCES

1 Davis, L. G., Goodwin, J. F., Steiner, R. E., and Van Leuven, B. D., *Brit. Heart J.*, 1953, **15**, 393.
2 Lodge, T., *Recent Advances in Radiology*, 1955. Churchill, London.
3 Grainger, R. G., and Hearn, J. B., *J. Fac. Radiol. (Lond.)*, 1955, **7**, 66.
4 Parker, F., and Weiss, S., *Amer. J. Path.*, 1936, **12**, 573.
5 Araujo, J., and Lukas, D. S., *J. clin. Invest.*, 1952, **31**, 1082.
6 Drinker, C. K., *Pulmonary Oedema and Inflammation*, 1945. Harvard University Press, Cambridge, Mass.
7 Hayward, G. W., and Knott, J. M. S., *Brit. Heart J.*, 1955, **17**, 303.

Diagnostic Pneumoperitoneum

SIR,—The paper by Drs. S. C. Truelove and K. Lumsden (*Journal*, September 3, p. 585) reminded us of our interest in this radiological and another technique (surgical)—that is, peritoneoscopy—in 1949–50, when, in the course of chest clinic practice, we were "refilling" patients who had therapeutic ("artificial") pneumoperitoneum (A.P.P.) for pulmonary tuberculosis. Abdominal palpation during A.P.P. treatment reveals the liver lying in mid-abdomen, its rounded upper surface recalling the sensation transmitted to the hand in palpating the uterine fundus in late pregnancy; in the left lateral decubitus its superior surface may readily be felt. The spleen was not usually palpable, probably as our patients mainly had spleens of normal size and diffluence.

Through the courtesy of Dr. R. Hermon, consultant radiologist, we obtained straight and lateral abdominal *x*-rays in a small series of tuberculosis patients who had A.P.P. These confirmed downward and medial displacement of liver and spleen, and, in cases of A.P.P. fortified by the effects of the operation of left phrenic crush, that the barium-filled stomach may be ptosed and contorted ("cascade-stomach"). It was surprising that such marked hepatoptosis and general visceroptosis either did not cause, or caused but minor, symptoms.

Although it was scarcely within our province, we became intrigued with the diagnostic possibilities of peritoneoscopy in various abdominal and pelvic conditions. In our scrutiny of the literature we learned that, among others, Mr. J. Ruddoch[1] and Mr. J. Hosford[2] had used the procedure, the latter advocating revival of interest in a technique first demonstrated in the U.K. as long ago as 1902. In peritoneoscopy, air is introduced as a preliminary into the peritoneum in order to view abdominal or pelvic organs through the peritoneoscope.

Your contributors favour the "horizontal-prone" position and state that abdominal *x*-rays in either lateral position are a useful supplement. In our experience, small as it was in the circumstances, better *x*-rays were obtained in the lateral positions to outline the size and shape of liver and spleen respectively. However, these were done in tuberculosis patients with established A.P.P., soon after refills of 1,500 c.c. of air into a peritoneal cavity containing perhaps 1,000 to 1,500 c.c. from previous refills. We suggest that, while it is unwise to introduce more than 1,000 c.c. at first, a refill of similar volume on the second or third day would be safe and yield even better *x*-rays than the authors present in their paper. Due to extensive peritoneal malignancies or adhesions resulting from tuberculous peritonitis or other causes, it may be difficult at times to insert air freely into the peritoneal space, or impossible to effect more than a localized air-pocket. In such cases, although rare, the authors' radiological technique would be invalidated.

Finally, reference is made to the sparse mention in standard textbooks of this technique. One of us (L. D.) in his book *Differential Diagnosis (Clinical and Radiological) in Chest Disease* (in German)[3] draws attention to its value where it is not easy to determine on straight chest skiagraphy if a shadow apparently in the lower thorax is, in fact, situated above the diaphragm.—We are, etc.,

LASAR DÜNNER.
R. HARDY.

Hull.

REFERENCES

1 Ruddoch, J. C., *Surg. Gynec. Obstet.*, 1937, **65**, 623.
2 Hosford, J., *British Medical Journal*, 1948, **2**, 348.
3 Dünner, L., *Klinische-röntgenologische Differentialdiagnostik der Lungenkrankheiten*, 1954, Stuttgart.

Neurosis in General Practice

SIR,—I would like to congratulate Dr. J. C. E. Pougher on his stimulating paper on "Neurosis in General Practice" (*Journal*, August 13, p. 409). Certain points, however, require discussion.

First, his statement that there have been few papers dealing with analysis of neurosis in general practice and nearly all have been American. To my own knowledge, not only have there been at least four such analyses in recent years —by Philip Hopkins in *Modern Trends in Psychosomatic Medicine*,[1] by J. Whitby in a recent discussion at the Royal Society of Medicine meeting,[2] by Arthur Watts in *Clinical Medicine in General Practice*,[3] and by myself[4]—but Drs. Betty and Arthur Watts have written an excellent book on this very subject.[5] Whilst the American papers may be appropriate to an analysis of American practice, we must be careful in applying these results to our own country, as there are many social dissimilarities.

Dr. Pougher's figure of 36.2% for the incidence of "neurosis" in general practice is high indeed, and his statement that these patients account for "more than 50%" of our time also seems excessively high when compared with other practices. Of course, all general practices are different, both in the different types of patient treated and in the different outlooks and views of the practitioner, and comparison may be rather false, but from other sources the figures for the incidence of neuroses all seem to be between 5% and 15% of the total numbers seen. May not this discrepancy be one of nomenclature rather than a difference in incidence? The criteria for labelling a patient as a "neurotic" differ from doctor to doctor, but it is very

important that we should have a precise and definite definition, as the label may become a very dangerous one and result in delaying or missing cases of organic disease under this loose and facile façade. Glancing through Dr. Pougher's list of symptoms, there are some that should merit the most careful consideration before such a diagnosis is made. Symptoms such as "dysphagia," "constipation," "abdominal pain," "chest pain," "diarrhoea," and others suggestive of a possible organic disorder must all be carefully investigated. I am sure that in this particular study all these did in fact turn out to be "neurotics," but it should serve as a warning that this diagnosis should be decided only after a careful clinical examination and after any other investigations which may be necessary. Again, Dr. Pougher's criteria for diagnosis may be rather ambiguous to the inexperienced. Atypical symptoms, whilst being suggestive of "neurosis" should also be a signal for the full use of all our diagnostic faculties to arrive at a correct diagnosis; all patients who seek our advice are anxious, some being more so than others, and whilst anxiety may be a feature of "neurosis" it may also accompany the organic condition. A dramatic description of the symptoms depends on the patient's personality and upbringing, and should not lead blindly to a diagnosis of neurosis. The past history is of importance, especially to the general practitioner, but we must always remember that our worst neurotics will eventually die from an organic condition, whose diagnosis may possibly be delayed if we pay too much attention to this past history.

All this is written not so much as criticism, but rather as a warning against a too facile tendency to diagnose "neurosis," and also to try and show that it should not naturally follow from Dr. Pougher's paper that our nation is one-third neurotic. In my experience it is rare to encounter patients in practice who are free from all of the so-called "neurotic" symptoms, but then how many of us all can truly say that we have not experienced identical symptoms ourselves?

One final point. I entirely agree with Dr. Pougher that the vast proportion of these patients can be managed by the practitioner himself—in my own practice only 7% require referral to the specialist—but at the same time the general practitioner must beware of undertaking too much and hanging on too long to the psychiatric patient who requires urgent and specialist treatment.—I am, etc.,

Beckenham, Kent. JOHN FRY.

REFERENCES

1 Hopkins, P., in O'Neill, D., *Modern Trends in Psychosomatic Medicine*, 1955. London.
2 Whitby, J., *Proc. roy. Soc. Med.*, 1954, **47**, 501.
3 Watts, C. A. H., in Fry, J., *Clinical Medicine in General Practice*, 1954. London.
4 Fry, J., *Med. Wld (Lond.)*, 1954, **80**, 657.
5 Watts, C. A. H., and Watts, B. M., *Psychiatry in General Practice*, 1953. London.

Food-poisoning

SIR,—Food-poisoning and its prevention excite a recurring interest each year. The handles of water-closets have always seemed to me not only unappetizing but dangerous. Would it not be a good idea, as new closets are made, to equip them with pedals?—I am, etc.,

Croydon. P. MESTITZ.

POINTS FROM LETTERS

Herpes Zoster and Chicken-pox

Dr. KENNETH SANDERS (London, N.W.10) writes: Further evidence of a common virus causing herpes zoster and chicken-pox is afforded by the following case. I recently attended a 78-year-old woman with herpes zoster affecting L.1. Twenty-two days after the first appearance of her rash her granddaughter, aged 2½, has produced the first crop of varicella lesions. The child is not a contact of any other possible source of infection, and indeed this is the only case of chicken-pox I have seen during the past two months.

Obituary

J. F. C. HASLAM, C.M.G., *M.C.*, M.D. F.R.C.P.Ed., D.P.H.

Dr. J. F. C. Haslam, formerly director of medical services of Northern Rhodesia, died in Cape Town on September 2. He was 67 years of age.

John Fearby Campbell Haslam was born at Rugby on June 13, 1888, the son of Mr. J. B. Haslam, and was educated at Dollar Academy and at Edinburgh University, where he graduated M.B., Ch.B. in 1912. Obtaining the D.P.H. of the Scottish Royal Colleges in 1920, he proceeded to the M.D. and was elected M.R.C.P.Ed. in 1924, being admitted a Fellow of the College in 1933. After graduation he held the appointments of house-physician and house-surgeon at Chalmers Hospital, Edinburgh, and later became assistant professor of forensic medicine in Edinburgh University. He served in the first world war as a captain in the R.A.M.C. in Salonika, Serbia, Palestine, and France, being awarded the Military Cross in 1918 for his services in Salonika, and mentioned in dispatches.

Haslam entered the Colonial Medical Service in 1921, when he was appointed assistant medical officer of health for British Guiana, becoming Government medical officer of health and port health officer for Georgetown in the following year. He left British Guiana in 1925 on being appointed assistant director of the Bureau of Hygiene and Tropical Diseases under the Colonial Office in London. After five years with the Bureau he became chief physician and bacteriologist with the Shell Company in Venezuela, but in 1933 he returned to the Colonial Medical Service as chief medical officer in Barbados, leaving there in 1935 to become director of medical services of Northern Rhodesia. While in the British West Indies he acted as honorary secretary of the Royal Sanitary Institute's board of examiners.

Haslam's wide experience proved invaluable in Northern Rhodesia, and for his work as director of medical services he was appointed C.M.G. in 1941. From 1947 to 1950 he was chairman of the Silicosis Medical Bureau, and from 1950 to 1952 a member of the Silicosis Commission. His drafting of the silicosis ordinances was a noteworthy achievement.

When the Federation of Rhodesia and Nyasaland was established in 1953 he became the first chairman of the African Affairs Board, a standing committee of the Federal Assembly. For his help in connexion with the successful launching of the new Federation he received the thanks of the Governor-General. Haslam retired from the position of director of medical services in 1949, and later became a specially appointed Member for Northern Rhodesia in the Federal Parliament of Rhodesia and Nyasaland. He held this position until December last year, when ill-health forced him to resign. A member of the British Medical Association for thirty-four years, Haslam was elected to the council of the British Guiana Branch in 1926, and to the presidency of the Barbados Branch in 1934 and of the Northern Rhodesian Branch in 1936. When the British Medical Association held its Annual Meeting at Edinburgh in 1927 he acted as one of the secretaries of the Section of Tropical Diseases. He made many friends in Northern Rhodesia and elsewhere, and all who knew him will mourn his death. He is survived by his widow, formerly Miss Edith Mackenzie, daughter of the Rev. N. K. Mackenzie.

IAN MACPHERSON, M.D., F.R.C.P.

The news of the death on September 12 of Dr. Ian Macpherson, assistant physician to the General Infirmary at Leeds and consulting physician to St. James's Hospital, Leeds, has brought a great sense of loss to a wide circle of colleagues and friends. He was 46 years of age.

Ian Macpherson was born at York on October 28, 1908, the son of the late Mr. James Macpherson, and was educated at the Archbishop Holgate School and at Leeds University, where he graduated M.B., Ch.B. in 1932. He proceeded to the M.D. in 1937, and took the M.R.C.P. in the same year. After graduation he held resident appointments at the General Infirmary at Leeds, where he was house-surgeon to Mr. P. J. Moir and to the late Mr. Harold Collinson. He then gained much valuable clinical experience as resident medical officer at St. James's Hospital before returning to his teaching hospital to work in the department of pathology. Later, he was appointed medical tutor. In 1938 Dr. Macpherson joined the Territorial Army and was attached to the 4th/1st Northern General Hospital, which in 1939 became the 18th General Hospital and with which he went to France in February, 1940. In May of that year he was evacuated through Boulogne and then served in Malta for three years during the period of the siege, and later in the Canal Zone as officer commanding the medical division of the 1st General Hospital, with the rank of lieutenant-colonel. He was demobilized in 1945, and in the following year was appointed assistant physician to the General Infirmary at Leeds.

During the nine years that followed he served the hospital with the utmost diligence and devotion, and there were few facets of hospital and medical school life in which he was not an interested and valuable participant. He did much for the nursing staff as lecturer and examiner, and for some years was editor of the *University of Leeds Medical Journal*. In 1950 he was elected F.R.C.P. He was a very hard worker, and, because of his obvious sincerity and his unfailing willingness to respond to their requests, he was in great demand for consultations by doctors and their families when they were ill. From his early postgraduate years he had acquired a leaning towards cardiology, and he developed this specialty in his hospital work and in his private practice. He was a member of the British Cardiac Society, of which he seldom missed a meeting, and in 1953 he spent some months in cardiological clinics in North America.

Macpherson was a good athlete, but had little time for activities outside his professional work. He was, however, a good cricketer with a wide knowledge of the game and an active member of the Northern Cricket Society. By nature rather reserved, he had a very keen sense of humour, which, coupled with his natural kindness and consideration, endeared him to his many patients and to his colleagues, by whom he will be greatly missed. In 1940 he married Miss Marie Jones, and she survives him with the three young children of the marriage.

By the death of Dr. CHARLES MARKS on August 16 South Shields has lost a popular and highly respected general practitioner. He was 75 years of age, and for the past three years had been confined to bed, latterly in hospital. Charles Marks was born at South Shields on September 30, 1879, the son of a boiler-maker. His early ambition was to become a chemist, but this idea was discarded while he was employed as dispenser-bookkeeper by a local doctor, and he decided on medicine as a career. Entering the Newcastle Medical School with the aid of a scholarship, he studied during the day and made up prescriptions and kept the books for his employer in the evening. He graduated M.B., B.S., with honours, at Durham University in 1910. He then settled in practice in his native town, later becoming honorary ear, nose, and throat surgeon and lecturer in medicine and surgery at Ingham Infirmary. For thirty years he was police surgeon for South Shields, and other appointments he held included those of honorary surgeon to the Volunteer Life Brigade, examiner in first aid for the Mercantile Marine, and lecturer to the ambulance teams at Harton colliery. A member of the choir of St. Michael's Church for more than forty years, he was the first president and conductor of the South Shields male voice choir, being re-elected president only last year. His third wife, formerly Miss Mabel Appleby, whom he married in 1948, survives him, together with his son, Dr. C. I. M. Marks, who has succeeded him in the practice, and his daughter, who is the wife of the Rev. A. L. Morrison, vicar of Christchurch, Gateshead.

The death on September 9, at the age of 70, of Dr. JAMES MCFARLANE at his home at St. Andrews has removed a practitioner who, in a quiet and an unobtrusive way, gave unstinted and skilful service to his patients in Hamilton, Lanarkshire, and, later, in near-by Chapelhall by Airdrie over a period of some forty years. James McFarlane was born on October 5, 1884, and studied medicine at Glasgow University, where he graduated M.B., Ch.B. in 1906. Before settling in practice at Hamilton about 1912 he had held the appointment of house-physician at Perth Royal Infirmary. After practising at Hamilton for some fourteen years he moved in 1926 to Chapelhall by Airdrie, where he remained until 1950, when he retired and went to live at St. Andrews. His sudden death occurred only a few days after he had submitted for publication in this *Journal* a short account of two cases of knotted cord (see page 851). Dr. McFarlane is survived by his widow and three daughters.

The news of the sudden death of Dr. CHARLES BATEMAN on September 10 at the early age of 53 was received with great regret by his colleagues in Preston and by his former patients, who were devoted to him. In the past few years Charles Bateman had to combat a serious heart condition, and he was forced to retire from practice six months ago. He returned to his native Westmorland, to Preston Patrick, near Milnethorpe, where he was born on October 17, 1901, the son of the late James Bateman, registrar for South Westmorland. He was educated at Heversham Grammar School and at Edinburgh University, where he graduated M.B., Ch.B. in 1923. He held resident house appointments in the Royal Surrey County Hospital, Guildford, and in the Preston Royal Infirmary before entering general practice in Preston nearly 30 years ago in partnership with Dr. Cedric Pimblett. His success as a general practitioner was marked not only by the large practice which he built, but by the gratitude and devotion of his patients, who expressed this in the presentation made on his retirement last March. Though he was of a quiet and retiring disposition he was popular with all his colleagues and beloved by all who knew him well. He loved an open-air life, playing golf or walking and climbing in his own Lake District. His home on retirement was among those hills, though he could no longer do any serious climbing. He was twice married and is survived by his widow and two sons and a daughter. He had attended the wedding of his elder son earlier in the day on which he died.—F. M. R.

Miss KATHLEEN LYNN, one of the founders of St. Ultan's Infant Hospital, Dublin, died in Dublin on September 14 at the age of 81. She was one of the first women in Ireland to graduate in medicine, and became a prominent personality in the medical and political life of Dublin. Kathleen Florence Lynn was born at Mullafarry, Co. Mayo, on January 27, 1874, the daughter of a Church of Ireland clergyman, and was educated at a school in Düsseldorf and

at Alexandra College, Dublin. As a young girl in the west of Ireland she saw a good deal of sickness and unhappiness caused by poverty, and this certainly had an influence on her future career. She enrolled at the old Royal University of Ireland as a medical student, and graduated M.B., B.Ch. in 1899. Ten years later she obtained the diploma of Fellowship of the Royal College of Surgeons in Ireland. After graduation she was elected to a post on the resident staff of the Adelaide Hospital, but the appointment of a woman provoked such strong opposition that she had to withdraw and became instead house-surgeon at the Royal Victoria Eye and Ear Hospital, Dublin, for a year. In 1902 she joined the staff of the Coombe Lying-in Hospital, which she continued to serve until 1916. The influenza epidemic of 1918 increased the volume of her work, and, to help combat the disease, with the help of a few other ladies she took over the old Domestic Training College in Dublin and after much hard manual work made it suitable for the admission of adult patients and, soon afterwards, of infants. In 1919 it was officially founded with the title of St. Ultan's Infant Hospital for the reception of children under 1 year of age, and from two cots in 1919 the hospital has grown to one with 90 beds. She had supported the republican movement in Ireland since 1912, and subsequently became surgeon-general to the Irish Citizen Army. During the Easter Week Rising in 1916 she attended the wounded in the Dublin City Hall and helped to negotiate the surrender of the garrison. She was sent to prison, first in Ireland and then in England, but was released in 1918 to help in the influenza epidemic. With the organization of the Sinn Fein movement in 1917 she was elected a member of its standing committee. In 1920 she was elected a republican member on the Rathmines Urban District Council, and three years later was returned as the republican representative of Dublin County in the first Dáil Eireann, but never took her seat. Her interest in the work of St. Ultan's Hospital remained undiminished with advancing age, and she was chairman of the board from 1945 until her death.

The memorial service for the late Provost R. M. F. Picken will be held on Sunday, October 2, at the Windsor Place Presbyterian Church, Cardiff, at 3.30 p.m.

Medico-Legal

WRONG INJECTION

A verdict of misadventure was returned at an inquest at Blackburn on September 13 on a baby aged 6 months who died after being mistakenly given an injection of mersalyl.

The child was taken by its mother on September 7 to the surgery of Dr. E. R. B. Murray, of Clitheroe. An appointment had been made for a diphtheria, whooping-cough, and tetanus prophylactic injection to be given. Mr. F. Morris, a qualified dispenser employed by the partnership of which Dr. Murray is a member, stated in evidence that he filled three syringes for injections—one of "cytamen," one of 2 ml. of mersalyl, and one of 2 ml. of combined diphtheria, whooping-cough, and tetanus vaccine. Following normal procedure he placed the three syringes on an instrument tray and called the doctor to give the injection to the child. The dispenser handed to Dr. Murray what he thought to be the syringe containing the prophylactic vaccine, and the contents were injected by the doctor into the child's buttock. After the mother and child had left the surgery the dispenser realized that he had handed the doctor the wrong syringe and that the child had been given 2 ml. of mersalyl. Later in the day she was admitted to hospital, where she died on September 11. The cause of death was given as uraemia due to renal failure due to an injection of 2 ml. of mersalyl. In his evidence, the paediatric senior house officer at the hospital said that he did not think that an antidote would have been effective unless it had been given almost simultaneously with the injection of mersalyl.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **September 10** (No. 36) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	6	1	2	0	1	12	0	2	0	
Dysentery	399	105	266	5	2	219	42	159	4	2
Encephalitis, acute	8	0		0		1	0	0	0	
Enteric fever:										
Typhoid	4	0	1	0	4	4	0	2	0	2
Paratyphoid	85	18	6	3		21	1	0	0	
Food-poisoning	897	82		1		336	21		3	
Infective enteritis or diarrhoea under 2 years				46	93				6	11
Measles*	1,663	38	35	25	50	1,083	57	134	35	19
Meningococcal infection	20	2	16	0		24	1	12	3	2
Ophthalmia neonatorum	33	2	8	0		30	1	2	0	
Pneumonia†	170	9	78	5		262	14	99	1	
Poliomyelitis, acute:										
Paralytic	206	26	78	5	7	47	0	12	0	2
Non-paralytic	252	31				31	2			
Puerperal fever§	227	22	7	2		210	21	10	1	
Scarlet fever	267	18	56	20	18	313	21	89	10	18
Tuberculosis:										
Respiratory	594	74	125	16		636	67	96	9	
Non-respiratory	74	8	26	8		106	8	19	3	
Whooping-cough	1,461	84	71	59	87	2,014	109	143	11	23

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	2	0	1	0	1		0	1	0	2
Influenza	1	0	0	0	0	3	1	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				1	0		
Pneumonia	113	12	9	6	4	108	21	7	7	2
Poliomyelitis, acute	6	0			0	2	0	1		0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	64	7	8	6	6	59	5	9	1	2
Non-respiratory		2	3	0	0		2	2	0	0
Whooping-cough	1	0	0	1	0	0	0	0	0	0
Deaths 0–1 year	156	22	27	7	23	180	13	11	9	3
Deaths (excluding stillbirths)	4,006	543	471	92	140	4,242	615	479	109	134
LIVE BIRTHS	6,976	1020	856	222	373	7,104	978	833	182	419
STILLBIRTHS	181	21	25			182	16	25		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

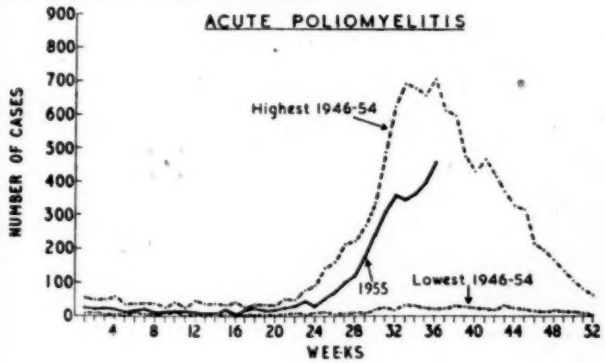
The uncorrected notifications of acute poliomyelitis in England and Wales for the week ending September 17 (37th week) numbered 411—a decrease of 47 on the previous week's total of 458. The proportion of non-paralytic cases (53.1%) again exceeded that of paralytic cases (46.9%), although not quite so markedly as in the 36th week, when the proportion of non-paralytic cases was 55%. The total uncorrected notifications in 1955, up to and including the 37th week, is 3,859. Notifications for the same period were more numerous in 1947 (5,599) and 1950 (5,614). Deaths from acute poliomyelitis in the great towns during the 37th week numbered 7 as compared with 6 in the previous week.

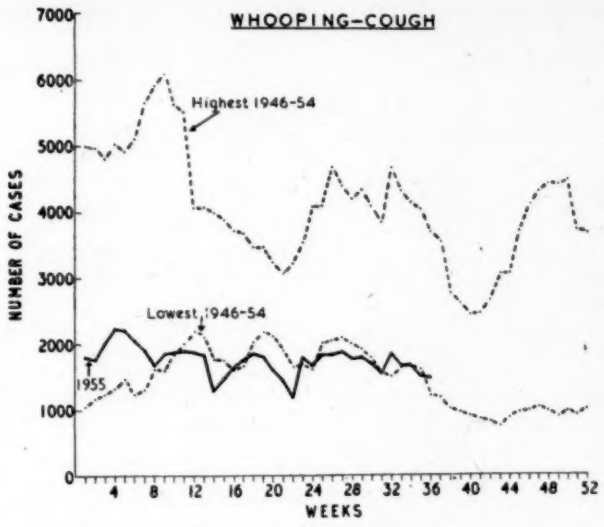
The figures for the 37th week show decreases in the London and south-eastern region (including Greater London) and the East and West Ridings, and also in the north-western, north midland, and southern regions. There were increases in the northern, eastern, south-western, and midland regions and in Wales. In the year to date the approximate incidence for England and Wales as a whole has been 8.7 per 100,000. On a county basis London, Essex, Middlesex, West Riding, Isle of Ely, and Buckinghamshire had the largest rates (13.6 to 18.6 per 100,000), followed by Gloucester, Kent, Somerset, Warwick, Hertford, Lincoln (Kesteven), Nottingham, Sussex (West), and Wiltshire (8 to 10 per 100,000). The following boroughs, etc., in England and Wales have had particularly high rates in the year to date (figures are for cases notified by September 17 with rate per 100,000 of the population in parentheses): Barnsley C.B. 73 (97.5); Hoyland Nether U.D. 12 (75.8); Willesden M.B. 133 (75.0); Wombwell U.D. 13 (69.2); Mexborough U.D. 12 (63.1); Dover M.B. 19 (55.8); Cheshunt U.D. 14 (55.2); Stepney Met.B. 49 (50.1); Marshland R.D. 8 (48.9); Poplar Met.B. 35 (48.8); Holborn Met.B. 11 (47.1); Clacton U.D. 11 (45.1); Thurrock U.D. 42 (43.3); Aylesbury M.B. 9 (42.4); Southwark Met.B. 40 (41.9); Worsborough U.D. 6 (41.8); Acton M.B. 25 (37.2); Rushden U.D. 6 (36.3); Lewisham Met.B. 81 (36.1); Wisbech M.B. 6 (34.9); Braintree R.D. 7 (34.9); Dewsbury C.B. 18 (33.9); Hammersmith Met.B. 36 (30.9).

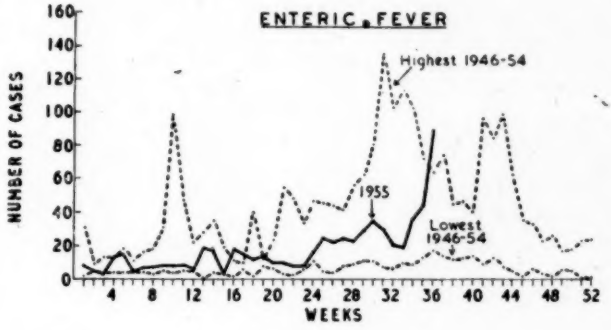
Scotland also showed a decrease in the number of notifications of acute poliomyelitis in the 37th week—64 as compared with 78 in the 36th week—the majority still being in Glasgow, which had a total of 39 cases. There was one death in Scotland.

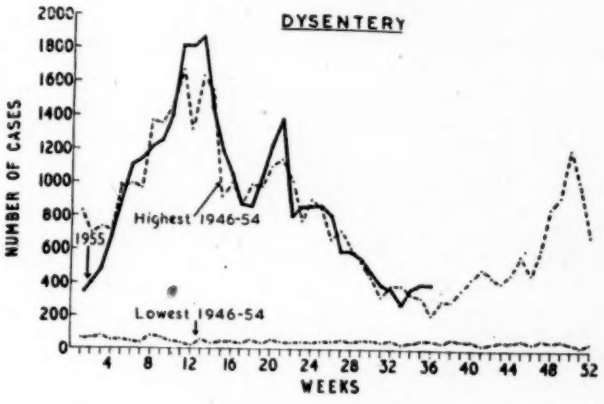
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1946–54 are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

In England and Wales, during the week ending September 10, the largest increases in the number of notifications were 337 for food-poisoning, from 560 to 897, 60 for acute poliomyelitis, from 398 to 458, 51 for paratyphoid fever, from 34 to 85, 39 for scarlet fever, from 228 to 267, and the largest decreases were 955 for measles, from 2,618 to 1,663, and 50 for whooping-cough, from 1,511 to 1,461.

The largest falls in the returns of measles were 88 in Devonshire, from 134 to 46, 65 in Lancashire, from 197 to 132, and 50 in Yorkshire West Riding, from 120 to 70. The most notable fluctuations in the trends of whooping-cough were a fall of 44 in the returns from Lancashire, from 223 to 179, and a rise of 37 in Northumberland, from 22 to 59. No large variations were reported in the local trends of scarlet fever. 6 cases of diphtheria were notified, the same number as in the preceding week.

Paratyphoid fever was mainly centred in two areas, Nottinghamshire 43 (Worksop M.B. 19, Kirby in Ashfield U.D. 16, Mansfield M.B. 4), and London 18 (Hackney 12, Shoreditch 5). The rise in London was mainly due to a

source of infection in a bakery and in Nottinghamshire to infected meat products.

399 cases of dysentery were notified, 1 fewer than in the preceding week. The chief feature of the returns was an increase of 52 in London, from 53 to 105. The largest returns during the week were London 105 (Chelsea 27, St. Pancras 27, Southwark 13, Islington 10), Lancashire 85 (Liverpool C.B. 28, Preston C.B. 12), Yorkshire West Riding 50 (Huddersfield C.B. 11, Leeds C.B. 11, Bradford C.B. 9), Warwickshire 16.

The largest outbreaks of food-poisoning were Lancashire 466 (Darwen M.B. 298, Accrington M.B. 78), and London 882 (St. Marylebone 56).

In Scotland the number of notifications of dysentery rose from 240 to 266. The largest centre of infection was Glasgow, with 182 notifications. An increase of 25 was recorded in the notifications of acute poliomyelitis, from 53 to 78. 48 cases were recorded in Glasgow.

Week Ending September 17

The notifications of infectious diseases in England and Wales during the week included: acute poliomyelitis 411, scarlet fever 329, whooping-cough 1,142, diphtheria 9, measles 1,038, acute pneumonia 164, dysentery 417, paratyphoid fever 115, and typhoid fever 4.

Outbreak at Royal Free

The obscure infectious disease causing an outbreak at the various branches of the Royal Free Hospital was reported in 5 new cases during the week ending September 26. Two of these were at Lawn Road Hospital and 3 at the Hampstead General Hospital. They comprised 3 nurses, 1 physiotherapist, and 1 domestic worker.

Medical News

British Council for the Welfare of Spastics.—The annual meeting was held at B.M.A. House on September 23 under the chairmanship of Mr. Paul Cadbury. Sir Frederick Messer, M.P., gave an address on "The Spastic and his Future." The council is a central advisory, co-ordinating, and consultative body for all activities affecting the welfare of spastics in Britain, on which are represented the main national medical, paramedical, educational, and other interested organizations. Last year the council completed the purchase and equipment of a permanent residential home in Buckinghamshire—"Ponds Home"—for 30 young spastics whose disability is so great that it precludes their employment. Dr. C. D. S. Agassiz is the warden, and so far 12 spastics have been admitted. In its report the council observes that cerebral palsy, from being a "Cinderella" problem a decade ago, has now achieved the widest public notice, largely owing to the efforts of the National Spastics Society during the last three years. The council is impressed by the need for accurate national statistics of the number of spastics over 16 years of age—the number of spastic children under 16 in England and Wales is between 6,000 and 10,000—as this lack "makes it particularly easy to exaggerate the size of the problem and to lose any sense of proportion."

Chartered Society of Physiotherapy: Diamond Jubilee Dinner.—The Chartered Society of Physiotherapy (see also p. 845) held its Diamond Jubilee Congress dinner at the Park Lane Hotel on September 22, with the president, Sir Cecil Wakeley, in the chair. The guests of honour were the Earl and Countess Mountbatten of Burma. The toast of the Society was proposed by the chairman of its council, Sir Harold Boldero. He sketched the growth of the Society, and, *pari passu*, of physiotherapy, over the 60 years. There were 4,000 physiotherapists working in the Health Service, and last year they treated 1¼ million patients. Now, as always, said Sir Harold, the essential aims of the profession were to attain proficiency and to follow its rules of conduct. Miss M. I. V. Mann, in reply, hoped that physiotherapists would always be worthy of the confidence placed by the medical profession in their competence, skill, and integrity. "Put us on our toes," she said, "and we will stay there." Sir Cecil Wakeley proposed the health of the guests. Earl Mountbatten, in response, gave what he termed a "lecture on physiotherapy" based on his obviously wide experience of many injuries and their treatment over the course of 34 years' polo playing. The audience greatly enjoyed the speaker's account of his experiences, as, indeed, Lord Mountbatten appeared to enjoy relating them, and his observations were acute to the extent of providing food for thought as well as pleasure. The Society held a reception and dance at Londonderry House, Park Lane, on September 23.

Endowment for Research on Schizophrenia.—Mr. Joseph Porton, of Leeds, has given £10,000 as an endowment fund for research prizes on schizophrenia. Awards, which will be made by a medical advisory board, are limited to teachers or graduates in psychiatry of Leeds University and the Hebrew University of Jerusalem. The entire capital sum will be awarded for the discovery of a "complete and permanent cure of schizophrenia" if made within the next five years; otherwise, after that time the money will be used for research fellowships. In the meantime, the income from the fund will provide two annual research prizes of not more than £250 each.

Horder Lecture.—At its meeting at Llandrindod Wells on September 23 the British Spas Federation decided to institute an annual lecture in memory of the late Lord Horder, who was the Federation's president for many years. The Horder lecture will be delivered by a distinguished physician or surgeon. Professor R. E. Tunbridge, professor of medicine at Leeds, was elected president of the Federation.

Midland Centre for Neurosurgery.—Members of the Second International Congress of Neuropathology and the Symposium Neuroradiologicum, which met in London last month (see this *Journal*, September 24, p. 784), were guests of the Midland Centre for Neurosurgery, Smethwick, on September 19. During the afternoon there was a symposium on the future of neurosurgery, neuroradiology, neuropathology, and neurology, at which the opening speakers were Sir Geoffrey Jefferson, F.R.S., Dr. J. W. D. Bull, Professor Alfred Meyer, and Dr. Macdonald Critchley. Several of the foreign visitors were concerned with the establishment of neurosurgical centres in their own countries, and they were particularly interested in the arrangements at Smethwick. The wives of the delegates were taken as guests of the West Bromwich and District Hospitals Management Committee on a tour of Stratford-upon-Avon during the afternoon; in the evening they were joined by their husbands for dinner and a performance of *All's Well That Ends Well* at the Shakespeare Memorial Theatre.

Malaria in Mexico.—The United Nations Children's Fund has allocated $2,400,000 to help eradicate malaria in Mexico. This is the largest single sum allocated by the Fund in its nine years' history. The money will be used for insecticides, transport, and other supplies in the Mexican Government's five-year campaign to protect the 17 million persons living in malarious areas.

Alcoholism in France.—Figures published by the French national institute of statistics for 1954 show the highest number of deaths from acute alcoholism yet recorded in France. Last year 4,106 people died from acute alcoholism, the rate in the Morbihan department, the worst affected, being 42 deaths per 100,000 inhabitants. There were 12,071 deaths from cirrhosis of the liver, which is also a record.

Dr. Alfred Torrie, formerly medical director of the National Association for Mental Health, has resigned his position as physician superintendent of The Retreat, York. He leaves early in the New Year.

UNIVERSITY OF MICHIGAN LIBRARIES

COMING EVENTS

Medical Protection Society.—Annual general meeting, October 5 at 3 p.m. at Victory House, Leicester Square, London, W.C.2.

Institute of Dermatology.—Semi-permanent exhibition on "Histology of Normal Skin," October 7–29.

London Hospital.—Old Students dinner, October 13 at the Trocadero Restaurant, 7 for 7.45 p.m. Tickets (32s. 6d.) from Dr. R. R. BOMFORD, 22, Harley Street, London, W.1.

St. Luke's Service.—The fifth annual service for doctors and nurses will be held at Norwich Cathedral on Sunday, October 16, at 3.30 p.m. The Dean will preach the sermon.

University College Hospital Medical School.—Annual dinner for past and present students, October 21 at the Savoy Hotel, 7.30 for 8 p.m. Tickets (30s.) from hon. secretary, Old Students' Association, University College Hospital Medical School, University Street, London, W.C.1. Postgraduate clinical demonstrations and lectures at the medical school, October 20 and 21.

Wessex Rahere Club.—Autumn dinner, October 29 at Fortt's Restaurant, Bath. Details from Dr. A. DAUNT BATEMAN, 11, The Circus, Bath.

London Marriage Guidance Council.—A course of four lectures for doctors on psychological problems in marriage, November 3, 10, 17, and 24 at 7 p.m. at 39, Queen Anne Street, London, W.1. Fee for course 1 guinea, for single lecture 7s. 6d. Apply to secretary, London Marriage Guidance Council, 78, Duke Street, London, W.1.

British Occupational Hygiene Society.—Autumn Conference on "The Use and Abuse of Protective Equipment" at the London School of Hygiene and Tropical Medicine on November 4, starting 11 a.m. Protection of the lungs, skin, eyes, and feet will be discussed. Details from hon. scientific secretary, M.R.C. Laboratories, Holly Hill, Hampstead, London, N.W.3.

London Medical Exhibition.—The exhibition will be held at the New Hall of the Royal Horticultural Society at Westminster from November 14 to 18. Sir CHARLES DODDS, F.R.S., will open the exhibition. Doctors who have not received invitations before November 4 should apply to the organizers, The British and Colonial Druggist Ltd., 194–200, Bishopsgate, London, E.C.2.

International Congress on Documentation of Applied Chemistry.—The congress will be held at the Institut Française du Royaume-Uni, Queensberry Place, London, S.W.7, from November 22 to 25. Details from the hon. secretary, 56, Victoria Street, London, S.W.1. In connexion with the congress there will be a special exhibition on books, periodicals, and documentation of applied chemistry at the Science Museum, South Kensington.

NEW ISSUES

Abstracts of World Medicine.—The new issue (Vol. 18, No. 3), which is now available, contains abstracts of important papers drawn from medical and other scientific journals published in some 20 different countries and in all five continents. The subjects covered range over the whole field of clinical medicine and include pathology, bacteriology, pharmacology, and chemotherapy; there are also sections dealing with medical genetics, public health and industrial medicine, forensic medicine and toxicology, anaesthetics, radiology, and the history of medicine.

Issued monthly; annual subscription £4 4s.; single copy 8s. 6d.; a specimen will be sent free on request to the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Ophthalmic Literature.—The new issues (Vol. VIII, No. 5, and Vol. IX, No. 1) are now available.

Ophthalmic Literature is a comprehensive abstracting journal covering ophthalmic journals from all countries of the world, articles of ophthalmic interest in journals devoted to general medicine and the other specialties, and those with an ophthalmological bearing which appear in journals dealing with such branches of the fundamental sciences as physiology, biochemistry, heredity, and anatomy.

Six issues and a volume index each year; annual subscription £4 4s. (or in combination with *British Journal of Ophthalmology*, £7 7s.); single copy 25s.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, October 3

INSTITUTE OF PSYCHIATRY.—5.30 p.m., Dr. E. Stengel: postgraduate lecture-demonstration.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. George Qvist: Acute Intestinal Obstruction; 6.30 p.m., Mr. V. H. Riddell: Treatment of Thyrotoxicosis.

Tuesday, October 4

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. C. O. Carter: Principles of Genetics.

MIDDLESEX HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. W. S. McCulloch (Mass.) and Dr. P. Wall (Harvard): Plotting of Pathways in the Central Nervous System. Action of Strychnine.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Professor C. G. Rob: Surgery of the Abdominal Aorta and its Major Branches; 6.30 p.m., Dr. W. G. Oakley: Surgery in the Diabetic.

Wednesday, October 5

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Role of Pyogenic Cocci in Skin Diseases

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Young: Pathogenesis of Tuberculosis (1).

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. Harland Rees: Differential Diagnosis of Frequency of Micturition.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Hugh Owen Thomas Memorial Lecture by Professor J. Trueta: Aetiopathology of Osteoarthritis.

MIDDLESEX HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. W. S. McCulloch (Mass.) and Dr. P. Wall (Harvard): Fate of Afferent Impulses in the Central Nervous System. Reflex Inhibition.

MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., Professor H. F. Humphreys: Some Reflections on World Health.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. P. H. Newman: Mechanical Derangement of Joints; 6.30 p.m., Mr. J. C. Ross: Indications for the Different Types of Prostatectomy.

●ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Professor S. G. Graham: Changing Paediatrics.

Thursday, October 6

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. O. S. Tubbs: Surgery of the Pericardium; 6.30 p.m., Mr. J. H. Doggart: Orbital Disease.

Friday, October 7

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. E. N. Wigley: clinical demonstration.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. L. Livingstone: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., Mr. N. Asherson: Vertigo.

OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 8.15 p.m., Professor Walter Artelt (Frankfort): Samuel Thomas von Soemmerring (1755-1830): a versatile scientist.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. E. L. Farquharson: Some Problems in the Treatment of Hernia; 6.30 p.m., Mr. Rainsford Mowlem: Reconstruction of the Jaws.

Saturday, October 8

BRITISH ASSOCIATION OF ALLERGISTS.—At King's College Hospital Medical School, S.E., 11 a.m., Autumn Meeting. Papers by Professor P. H. Gregory, Dr. J. M. Hirst, Miss D. Hamilton, Dr. Kate Maunsell, Dr. J. L. Livingstone, Dr. E. Marley, and Dr. B. S. Cardell.

BIRTHS, MARRIAGES, AND DEATHS

MARRIAGES

Cantwell—Boswell.—On September 10, 1955, at St. Mary's, Croydon, Surrey, Ronald J. Cantwell, M.B., Ch.B., D.C.H., to Patricia M. Boswell, N.Z.R.N., both of Auckland, New Zealand.

Staniland—Mathias.—On September 24, 1955, at St. Gabriel's Church, Cricklewood, London, N.W., Gerald Cedric Staniland, M.Sc., M.B., Ch.B., F.R.C.S., to Shelagh Mathias, M.B., B.S.

Stewart—Haworth.—On September 21, 1955, at St. James Church, Thornham, Rochdale, Lancs, Alexander Stewart, M.B., Ch.B., of "Corrour," Manchester Road, Chapel en le Frith, Derbys, to Ann Shirley Ramsden Haworth, M.S.R.(T.), of 4, Tandle Hill Road, Royton, Lancs.

DEATHS

Cassell.—On September 8, 1955, at Dorrington House, Dorrington, near Shrewsbury, Salop, Charles William Cassell, M.D., D.T.M.

Clarke.—On September 8, 1955, at 47, Gravelly Hill North, Birmingham, Lionel Beale Clarke, L.M.S.S.A., Lieutenant-Colonel, R.A.M.C., retired, aged 67.

Harcourt.—On September 4, 1955, George Robert Harcourt, M.B., of 6, Norman Avenue, Abingdon, Berks, formerly of Leyton and Loughton, Essex, aged 85.

Hickinbotham.—On September 1, 1955, at West Bergholt, Essex, James Ryland Hickinbotham, M.B., aged 85.

Hugh-Musgrove.—On September 8, 1955, at West Middlesex Hospital, the result of an accident, Sheila Mary Helen Hugh-Musgrove, M.B., B.S.

McMurtrie.—On September 4, 1955, at North Berwick, Alexander Church Brodie McMurtrie, *M.C.*, M.D., F.R.C.S.Ed., D.P.H., of Orchard House, Carleton, Carlisle, Cumberland.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Albuminuria in Recruits

Q.—*What is the best laboratory test in assessing fitness for military service in young men who show traces of protein in their urine and are referred to the pathologist? The urea clearance test has on several occasions shown grossly defective renal function in men who, a year or two later, have not shown any clinical evidence of kidney disease.*

A.—Benign orthostatic albuminuria may be diagnosed on the *absence* of albumin in a specimen of urine passed on rising from bed in the morning, the bladder having been emptied on retiring. If no fluids have been taken after 4 p.m. the day before, the specific gravity of this night urine may be a useful index of renal concentrating power. A specific gravity of 1024 or more would be a satisfactory result. The urea clearance test has a wide range of "normality" from 50% to 150% of the mean value in health. The occasional low figures should not be taken too seriously and errors can readily creep in from failure to empty the bladder properly and other technical faults. Proteinuria may occasionally be found as the residue of an acute nephritis which is clearing up. In true chronic Bright's disease albuminuria is *persistent*.

Chloramphenicol and Aplastic Anaemia

Q.—*When is it justifiable to use chloramphenicol, in view of the risks of aplastic anaemia? Is there a dangerous duration or level of dosage which should not be exceeded from this point of view? Do any of the other newer antibiotics carry an appreciable risk of this complication?*

A.—The only condition in which chloramphenicol is irreplaceable is enteric fever. Although approximately equivalent in activity to other broad-spectrum antibiotics for many other purposes, it may be preferred to them (*a*) in the treatment of meningitis, especially that due to *H. influenzae*, because of its greater capacity to penetrate the blood–brain barrier, (*b*) for whooping-cough, because of somewhat superior therapeutic action, (*c*) for infections by staphylococci when the organism is resistant to penicillin and the tetracyclines, (*d*) in some circumstances because its use is less liable than that of the tetracyclines to be followed by intestinal superinfection.

It is generally agreed that chloramphenicol should not be prescribed without good reason or for any trivial indication, but whether its use should be avoided whenever another drug will serve as well or nearly as well is a question on which there are two opposite opinions. Some practitioners and hospitals continue to use it freely, having been so fortunate as to have seen no ill effects: others whose experience has been less happy have abandoned its use except for imperative indications. Examples of authors whose colleagues have followed the latter policy are Needham and Nicholls,[1] of the Mayo Clinic, and Kirby and Ahern,[2] of Seattle: each of these papers records a diminution in the frequency of staphylococcal resistance to the drug consequent on the much-reduced scale of its use since its effects on the marrow were recognized. There is also much difference of opinion on the frequency of marrow complications. It is not known how many such cases have been undiagnosed, or if diagnosed unrecognized as having been caused by the drug. Even supposing the truth in this matter could be known, no one has ventured to suggest a numerical limit to the justifiable risk: for instance, if aplastic anaemia occurred in 1 case in 5,000, should the drug be used for ordinary purposes or not?

Excessive dosage is probably more dangerous: the limit suggested by Hodgkinson[3] is a total of 26 g. for adults, treatment not being continued beyond 10 days; or 100 mg. per kg. body weight daily for 7 days in children. Prolonged administration should certainly be avoided, and it is likely that a second course involves more risk than the first. On the other hand, according to many records, aplastic anaemia has resulted from the use of quite small amounts of the drug: some degree of risk, however small, is thus inevitable.

No other antibiotic possesses the nitrobenzene radical to which marrow effects are attributable, nor has any other been known to produce them, except in such rare instances that the association may have been coincidental.

References

1 Needham, G. M., and Nicholls, D. R., *J. Lab. clin. Med.*, 1953, **43**, 150.
2 Kirby, W. M. M., and Ahern, J. J., *Antibiot. and Chemother.*, 1953, **3**, 831.
3 Hodgkinson, R., *Lancet*, 1954, **1**, 285.

Abrams's Box and Joanna Southcott's Box

Q.—*In your obituary notice of the late Lord Horder (August 20, p. 493) mention is made of Abrams's box and the box of Joanna Southcott. What were these, and are there modern equivalents?*

A.—(1) Albert Abrams was born in San Francisco in 1863 and died there in 1924. He was M.D. Heidelberg. He introduced his theory of electronic reactions in 1916.[1] Its method of application was to connect a resistance coil with two electrodes and to place one electrode over the stomach and the other over some other part of the body. A contraction of the stomach, indicating the passage of a current, was termed a positive reaction. This contraction was measured by percussion. A moderate resistance in the circuit abolished the reaction, but a further increase in the resistance produced a sudden positive reaction. The ohmage at which the reaction became positive was called the "vibration rate," said to be constant for each individual, organ, and disease. The current measured by the resistance coil was termed an "electronic vibration." Abrams later dispensed with the patient, and his final method of diagnosis lay in placing a drop of blood, a smear of saliva, or the patient's signature in a box called a "dynamizer." The dynamizer was provided with an electrode which was placed on the forehead of a healthy subject. From areas of dullness elicited by percussion of the healthy subject's abdomen Abrams diagnosed the patient's disease. The electronic emanations said to cause the abdominal dullness were termed "Abrams reactions."

Abrams further concluded that disease was merely the expression of a certain vibratory rate, and that it could be cured by imposing on it a similar vibratory rate. For this purpose he devised the "oscilloclast," reducing diagnosis and treatment to a final simplicity. The diagnostic machine furnished the vibratory rate and the oscilloclast produced a curative vibratory rate. His theories and apparatus were investigated in 1924 by a small committee led by the late Lord Horder, whose findings, fully reported in the *Journal*,[2] conclude: "The conclusions arrived at in this Communication leave the position of the practising electronist as scientifically unsound and as ethically unjustified as it was before. They give no sanction for the use of E.R.A. [electronic reactions of Abrams] in the diagnosis or treatment of disease." Sir James Barr[3] and G. L. Scott[4] were both advocates of the method, but M. Fishbein[5] published a severely critical account.

Claims are still made periodically on behalf of dubious "electronic" devices for the diagnosis and treatment of disease.

(2) Joanna Southcott (1750–1814) was born in Devon and worked as dairymaid, domestic servant, or upholstress until she was over 40. In 1792, claiming to be divinely visited and chosen to warn the world of the imminence of the "second coming," she began prophesying in prose and verse. Her writings were first published in 1801 and brought her

many adherents. The term "Joanna Southcott's box" follows from her practice of placing her writings in boxes, only to be opened when the events predicted matured and at the demand of the Anglican bishops. Three that have been opened held nothing of real value, another some interesting Southcottian manuscripts. Various rival boxes have appeared, probably owing to the existence of boxes of relics belonging to old believers.

REFERENCES

1 *New Concepts in Diagnosis and Treatment.* San Francisco, 1916.
2 *British Medical Journal*, 1925, 1, 179.
3 *Abrams' Methods of Diagnosis and Treatment.* London, 1925.
4 *The Abrams' Treatment in Practice.* London, 1924.
5 *The Medical Follies.* New York, 1925, p. 99.

Laboratory Diagnosis of Poliomyelitis

Q.—*What laboratory tests are available to confirm a suspected diagnosis of acute poliomyelitis? How quickly can a report be expected and how reliable is it likely to be? Are such tests helpful in practice in the diagnosis of both the pre-paralytic case and the non-paralytic case, and will they distinguish susceptible from immune persons in a family which has been exposed to infection?*

A.—Hospital laboratories can examine cerebrospinal fluid by simple film and biochemical tests. This is of great value in distinguishing bacterial and especially tuberculous meningitis from virus meningitis, but these tests seldom provide information of much help in the differential diagnosis of the various causes of virus meningitis. Cell counts tend to be lower in poliomyelitis than in other forms of virus infection, but there are wide variations from case to case.

Virus laboratories can offer two main tests in suspected poliomyelitis infections : (1) tests for the presence of poliomyelitis virus in the stools or nasopharyngeal washings; and (2) serological tests for the presence of poliomyelitis antibody in the blood.[1]

Stools provide a more reliable source of virus than nasopharyngeal washings, as virus is present in the latter for a few days only, and often prior to the onset of recognizable symptoms. Virus is present in the stools at, or soon after, the onset of symptoms and persists in some cases for 12 weeks or longer. Isolation of virus is nowadays carried out in tissue cultures, and, given optimum laboratory conditions, a positive answer may be arrived at in seven to twelve days. Simple isolation of a viral agent in the stool can be carried out in two to four days, but this agent has to be typed by neutralization with type-specific serum before a diagnosis of poliomyelitis can be made, and this may take upwards of twelve days. The absence of virus from the stools cannot be firmly stated in less than 30 days, as serial passage in tissue culture must be done and the cultures observed for two to four weeks.

Serological testing of a single blood sample for the presence of poliomyelitis neutralizing antibodies is of little value, as antibodies indicate only that infection has occurred at some time. Comparison of acute and convalescent serum gives more accurate information, but antibodies to the infecting virus are known to be present in a significant titre even at the time of onset of paralysis. In the acute stage the serum should be collected as soon as possible and not later than four days after the onset of symptoms. The convalescent serum is collected 21–28 days after onset. Demonstration in the convalescent serum of a significant rise in antibody titre to one of the three types of poliomyelitis virus is an indication that the suspected illness was in fact poliomyelitis, even when the virus may not have been isolated from the stools. Complement-fixing antibody tests can also be used in diagnosis, but these are still in the developmental stage. It appears that the complement-fixing antibody does not persist for as long as the neutralizing antibody.

Because of the time factor, these tests do not help in the diagnosis of pre-paralytic cases, but they can be of help in confirming the diagnosis of nonparalytic cases. Likewise they are of little value in distinguishing susceptible from immune contacts, since the time taken to test the contact's serum for the presence of neutralizing antibodies detracts from the help that can be given to the clinician.

REFERENCE

1 *Poliomyelitis.* World Health Organization Monograph Series. No. 26. 1955. Pp. 237-67.

Cortisone and Corticotrophin in Pregnancy

Q.—*Is the administration of cortisone or corticotrophin during pregnancy likely to have an ill effect on the foetus? A patient of mine had 150 mg. of cortisone on alternate days for a month on account of severe nickel dermatitis. At the time of commencing treatment, but unknown to the hospital or myself, she was six weeks pregnant.*

A.—There is no point in telling this patient that her treatment may have had an ill effect on her baby; and, if she asks a leading question on the matter, she should be reassured. For, although the injection of cortisone into pregnant rabbits and mice has produced both intrauterine death and congenital malformations in the young, the writer is not aware of any similar report in the human. This is probably partly because the dosage used on these animals was, in proportion to their body weight, very much greater than that given therapeutically in man, and partly because data from experimental animals do not always apply to the human. Marquis and Hodgkinson[1] used corticotrophin and cortisone in 28 pregnant women, and found no increase in the incidence of abortion nor any physical or mental abnormality in the infants. Others[2 3 4] have reported to the same effect, although they advise the avoidance of large doses of the hormones in early and late pregnancy.

Babies delivered of mothers receiving, or having lately received, cortisone may show at birth withdrawal symptoms suggestive of under-activity of the adrenal cortex and require treatment. It seems likely that this occurs only when the mother is being given cortisone in the presence of an adequate endogenous production of corticosteroids, and not when it is being administered as replacement therapy for a maternal deficiency.

REFERENCES

1 *Obstet. Gynec.*, 1953, 1, 276.
2 Barnes, A. C., ibid., 1954, 3, 322.
3 Jones, G. S., and Howard, J. E., *New York St. J. Med.*, 1953, 53, II, 2463.
4 De Costa, E. J., *J. Mich. med. Soc.*, 1953, 52, 613.

Diagnosis of Anaemia after Initial Treatment

Q.—*Some anaemic patients sent to see me at hospital have already received treatment, perhaps for several months. Liver preparations or vitamin B_{12} have commonly been given. What is the correct management of such patients in order to make a diagnosis? Is it safe to discontinue treatment? In cases of pernicious anaemia how long does the marrow take to revert to a megaloblastic state after treatment is discontinued?*

A.—An anaemia which does not respond to adequate doses of liver preparations, vitamin B_{12}, or folic acid is most unlikely to be pernicious anaemia. A sternal puncture should be done, and megaloblasts will be found if the patient has pernicious anaemia or an allied dyshaemopoietic anaemia. The real difficulty arises when the patient is no longer anaemic. Is this pernicious anaemia in remission, or did the patient never have pernicious anaemia at all? The first thing to do is to carry out a histamine test meal. The presence of free acid rules out the diagnosis of pernicious anaemia. If there is achlorhydria after histamine, the diagnosis remains in doubt, for many elderly people have achlorhydria. A normal level of pepsin in the gastric juice or uropepsin in the urine will still rule out pernicious anaemia. Two other tests remain which can be carried out only in specially equipped centres. The first is the estimation of the absorption of radioactive vitamin B_{12} given by mouth; normal absorption rules out pernicious anaemia. The second is gastric biopsy; simple atrophy of the mucosa is more or less pathognomonic of pernicious anaemia.

If the patient can remain under observation, it is quite safe to discontinue therapy and watch the blood. The red cells will commonly begin to fall within two or three months, but relapse may be delayed for two or three years, and therefore a clean bill of health should not be given prematurely. The marrow may revert to the megaloblastic state within ten days or a fortnight of stopping treatment, but in some cases reversion must take very much longer. It is therefore easier to follow the blood than the marrow, and it is rarely worth examining the marrow until the haemoglobin has fallen to 75% or lower.

NOTES AND COMMENTS

Prognosis in Aplastic Anaemia.—Dr. A. Hill (Western Australia) writes: In your answer to the question on the treatment of aplastic anaemia ("Any Questions?" May 28, p. 1353) the great distress to which a patient was exposed by frequent blood transfusions for this condition is mentioned. A recent case treated by oral hydrocortisone is enlightening. Little is known here of aplastic anaemia and its treatment, and the case went undiagnosed for at least two years. During the latter one and a half years several courses of liver injections, vitamin B_{12}, and folic acid gave absolutely no relief—the patient became weak and breathless, pallor was marked, and he lost a stone in weight. The Hb fell to 27% and blood transfusion became an urgent necessity. Relief was obtained for but two to three weeks, so that repeated transfusions were needed, unless 3 to 4 pints (about 2 litres) were transfused, when a little longer relief was obtained. It was at this stage (after the diagnosis having been confirmed by rib resection) that oral hydrocortisone was commenced. At first one 20-mg. tablet was given 6-hourly for about a month, later reduced owing to palpitations; no other side-effects were observed. Transfusions became absolutely unnecessary and the patient regained normal weight and health, and Hb has steadily improved and is now 81.2% on 30 mg. oral hydrocortisone daily.

Date	*Hb%*	*Daily*
May 6, 1955		Last transfusion 2 pints (1.1 litres)
10	78	40 mg. oral hydrocortisone
24	68	" " " "
June 7	66	" " " "
21	60	" " " "
July 5	66	" " " "
19	72	30 mg. " "
26	74	" " " "
Aug. 9	72	" " " "
23	81.2	" " " "

Our Expert writes: The results of the treatment of aplastic anaemia with cortisone or hydrocortisone are almost invariably disappointing if there is a generalized hypoplasia of the marrow. Nevertheless, the drugs undoubtedly should be given a trial. When the hypoplasia is confined to the red-cell series, so-called "pure red-cell anaemia," the results of treatment seem more likely to be favourable.

A Good Head of Hair and Cancer.— Dr. B. Juhn (Walthamstow) writes: With reference to the question: "Is there a recognized relationship between growth of hair and the liability to cancer?" ("Any Questions?" September 17, p. 748), I would like to make the following addition. Professor Otto Lubarsch (1860–1933), a pupil of Virchow, put on record that in cases of cancer of the stomach the majority had a good head of well-pigmented hair. Lubarsch was editor of *Virchow's Archiv für Pathologische Anatomie*; with Henke of *Handbuch der Speziellen Anatomie und Histologie*; with Ostertag of *Ergebnisse der Allgemeinen Pathologie*. However, I regret that I have been unable to trace the paper mentioned above, which was published more than 30 years ago.

Hiccup during Anaesthesia.—Dr. F. F. Waddy (Northampton) writes: Your expert's reply to the question on hiccup during anaesthesia ("Any Questions?", August 13, p. 447), although not wrong in any sense, seems to me to require a little enlargement. It is true that in deep ether anaesthesia hiccups can be cured by the administration of carbon dioxide in most instances, and your expert is probably right in saying that in these cases it was insufficient depression of reflex irritability. In this instance increase in the depth of anaesthesia will also answer the purpose as a rule. On the other hand, there appears a very different cause of hiccups which I look upon as an incoordination of respiratory movements. This is sometimes manifest under a reasonable depth of curarization, when the intercostals seem to be paralysed but the normal movement of the diaphragm does not adequately expand the thoracic cavity. In these circumstances it is far better to depress the "respiratory attempt" centrally than to paralyse it peripherally with further curarization. In these instances an intravenous dose of pethidine is invaluable. Incidentally, in intractable hiccup in the conscious state pethidine is successful probably more often than any other drug.

Choice of Local Analgesic.—Dr. Victor Goldman (London) writes: In reply to a question concerning the "Choice of Local Analgesic" ("Any Questions?" September 3, p. 629) your expert states "in each case adrenaline is added to the solution in a concentration of 1 in 200,000." As your correspondent requested information concerning operations on the fingers, I feel that he should have been warned that adrenaline should not be used when operating on any extremity for fear of a subsequent gangrene.[1] As a matter of fact I have produced a profound degree of analgesia on one of my own fingers which lasted well over an hour by means of an "annular block" using less than 5 ml. of a 0.5% solution of lignocaine without any vasoconstrictor—so adrenaline in such a case is hardly necessary. Most authorities also state that adrenaline should not be added to an analgesic solution when the patient has advanced cardiac disease or thyrotoxicosis,[2] a fact which should be made known to all who would operate under local analgesia.

References

1 Adriani, J., *Techniques and Procedures of Anaesthesia*, 1947, p. 204, Blackwell.
2 Pitkin, G. P., *Conduction Anesthesia*, 1953, p. 441, Lippincott.

Treatment of Coccydynia.—Mr. F. C. Durbin (Exeter) writes: I find it difficult to agree entirely with the treatment of coccydynia advocated in "Any Questions?" (September 3, p. 629). It is admittedly a difficult condition to treat, but we need not be defeatist about it. The most resistant cases are those without a history of trauma, as in them it is not always possible to discount neurosis or perhaps disk degeneration and prolapse, and then local treatment may not always be successful. With a firm history of trauma, with pain on moving the sacro-coccygeal joint on rectal examination, treatment I would say is invariably successful. If conservative measures, including manipulation under anaesthesia and injection of local analgesics, do not bring relief, I have no hesitation in excising the coccyx, provided that (1) haemorrhage is adequately controlled; (2) tension sutures are inserted and tied over a gauze pack, to obliterate dead space and prevent haematoma formation; (3) antibiotics are administered post-operatively. There are rarely complications and the wound heals by first intention. If cases are carefully selected, the operation only occasionally fails to bring relief. If treatment is delayed for a considerable time, the development of psychological fixation may obscure the real organic basis of the complaint and render any form of therapy more uncertain of cure.

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